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(54) Title: ANTIBACTERIAL TARGETS IN ALLOIOCOCCUS OTITIDIS

(57) Abstract: The present invention relates to the identification of polynucleotide sequences encoding polypeptides of *Alloiococcus otitidis* that are essential for the growth and survival of the bacteria. In particular, the invention relates to polypeptides encoded by the *Alloiococcus otitidis* open reading frames (ORFs), and to their use in pharmaceutical compositions, therapeutics, diagnostics and the like. The present invention also relates to methods for identifying pharmaceutical compounds that inhibit the activity of the polypeptides that are essential for the growth of *Alloiococcus otitidis*, to pharmaceutical compositions containing these compounds and to their use in treatment and amelioration of diseases caused by *Alloiococcus otitidis*

ANTIBACTERIAL TARGETS IN ALLOIOCOCCUS OTITIDIS

FIELD OF THE INVENTION

The present invention relates to the genomic sequence of *Alloiococcus otitidis*
and polynucleotide sequences encoding polypeptides of the Gram-positive
bacterium, *Alloiococcus otitidis*. The invention also relates to polynucleotides and
polynucleotides encoding polypeptides, preferably antigenic polypeptides, encoded
by the *Alloiococcus otitidis* open reading frames and the uses thereof.

BACKGROUND OF THE INVENTION

Since the discovery of penicillin, the use of antibiotics to treat the ravages of
bacterial infections has saved millions of lives. With the advent of these "miracle
drugs," for a time it was popularly believed that humanity might, once and for all, be
saved from the scourge of bacterial infections. In fact, during the 1980s and early
1990s, many large pharmaceutical companies cut back or eliminated antibiotics
research and development. They believed that infectious disease caused by bacteria
finally had been conquered and that markets for new drugs were limited.
Unfortunately, this belief was overly optimistic. The tide is beginning to turn in favor of
the bacteria, as reports of drug resistant bacteria become more frequent. The United
States Centers for Disease Control and Prevention announced that one of the most
powerful known antibiotics, vancomycin, was unable to treat an infection of the
common bacterial pathogen, *Staphylococcus aureus*. This organism, commonly
found in our environment, is responsible for many nosocomial infections. The import
of this announcement becomes clear when one considers that vancomycin was used
for years to treat infections caused by Staphylococcus species as well as other
stubborn strains of bacteria. In short, bacteria are becoming resistant to our most
powerful antibiotics. If this trend continues, it is conceivable that we will return to a
time when what are presently considered minor bacterial infections are fatal
diseases.

Over-prescription and improper prescription habits by some physicians have
caused an indiscriminate increase in the availability of antibiotics to the public. The
patients are also partly responsible, since they will often improperly use the drug,

thereby generating yet another population of bacteria that is resistant, in whole or in part, to traditional antibiotics.

The bacterial pathogens that have haunted humanity remain, in spite of the development of modern scientific practices to deal with the diseases that they cause. Drug resistant bacteria are now an increasing threat to the health of humanity. A new generation of antibiotics is needed to once again deal with the pending health threats that bacteria present.

As more and more bacterial strains become resistant to the panel of available antibiotics, new antibiotics are required to treat infections. In the past, practitioners of pharmacology relied upon traditional methods of drug discovery to generate novel, safe and efficacious compounds for the treatment of disease. Traditional drug discovery methods involve blindly testing potential drug candidate- molecules, often selected at random, in the hope that one might prove to be an effective treatment for some disease. The process is painstaking and laborious, with no guarantee of success.

Newly emerging practices in drug discovery utilize a number of biochemical techniques to provide for directed approaches to creating new drugs, rather than discovering them at random. For example, gene sequences and proteins encoded thereby that are required for the proliferation of a cell or microorganism make excellent targets since exposure of bacteria to compounds active against these targets would result in the inactivation of the cell or microorganism. Once a target is identified, biochemical analysis of that target can be used to discover or to design molecules that interact with and alter the functions of the target. Use of physical and computational techniques to analyze structural and biochemical properties of targets in order to derive compounds that interact with such targets is called rational drug design and offers great potential. Thus, emerging drug discovery practices use molecular modeling techniques, combinatorial chemistry approaches, and other means to produce and screen and/or design large numbers of candidate compounds.

Nevertheless, while this approach to drug discovery is clearly the way of the future, problems remain. For example, the initial step of identifying molecular targets for investigation can be an extremely time consuming task. It may also be difficult to design molecules that interact with the target by using computer modeling techniques. Furthermore, in cases where the function of the target is not known or is

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poorly understood, it may be difficult to design assays to detect molecules that interact with and alter the functions of the target. To improve the rate of novel drug discovery and development, methods of identifying important molecular targets in pathogenic cells or microorganisms and methods for identifying molecules that
5   interact with and alter the functions of such molecular targets are urgently required.

The present invention is directed to identifying important molecular targets in a recently identified bacteria, *Alloiococcus otitidis,* which has been implicated in otitis media with effusion (OME). Otitis media, an inflammatory disease of the middle ear, is the most frequent cause of visits to pediatricians' offices in the United States
10   (Schappert, 1991). Approximately 80% of all children experience at least one episode of otitis media by the age of three (Klein, 1994). There are three main types of otitis media: Acute otitis media (AOM), otorrhea, and otitis media with effusion (OME). *Alloiococcus otitidis* has only been associated with otitis media with effusion (OME), but this may be due to the difficulty of its detection by standard bacterial culturing
15   methods. Its detection in the effusions is likely due to the fact that the effusions are normally sterile and few or no competing bacterial species are isolated from them. Without the interference of faster growing nasophryngeal species, the culture plates can be incubated for the longer duration needed to detect *Alloiococcus otitidis* colonies.

20   Three other bacterial species are commonly isolated from middle ear effusions. These are nontypeable *Haemophilus influenzae, Moraxella catarrhalis*, and *Streptococcus pneumoniae*. One or more of these species have been found in one study to be associated with about 77% of all cases of OME using a PCR detection method (Post, 2000). This study did not include assaying for *Alloiococcus otitidis*, so
25   a portion of the unaccounted cases may be due to this organism.

The bacterium *Alloiococcus otitidis* was first isolated from the middle ear fluids of 10 children in the Buffalo, NY area with persistent OME and characterized as a large catalase negative, Gram-positive cocci that tend to occur in clumps, often in tetrads. It is slow growing and requires 2 to 5 days at 37°C before colonies can be
30   seen on sheep blood agar plates. The bacterium was named *Alloiococcus otitis* by Aguirre and Collins (1992), who showed that it was different from other known Gram-positive species based on its 16S rRNA sequence. The bacterium's name has been

changed from *Alloiococcus otitis* to *Alloiococcus otitidis.* (Hendolin, et al., (1999), and Hendolin et al., (2000)).

Several studies of the epidemiology *Alloiococcus otitidis* indicate it is associated with otitis media with effusion. These are summarized in Table 1. These
5   studies have been done using both culture and PCR techniques. The number of cases detected by culture, as might be expected from the fastidious growth requirements of the bacterium, was less than the number detected by PCR. Assuming that the bacterium is detected more accurately by the PCR method, the bacterium is detected in between 10 and 50% of patients with OME. This frequency
10   suggests that this organism represents a significant public health problem. Consequently, there is a need for identifying gene targets in *Alloiococcus otitidis* for the development of anti-infectives. There is also a need for compositions for diagnosing *Alloiococcus otitidis* infection.

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TABLE 1: SUMMARY OF STUDIES INDICATING AN ASSOCIATION OF ALLOIOCOCCUS OTITIDIS WITH OTITIS MEDIA WITH EFFUSION (OME).

% detected	N^a	Method	Reference
8	200	Culture	Faden & Dryja, J. Clin. Microbiol. 27:2488 (1989)
3	100	Culture	Sih et al., ICAAC (1992)
20	25	PCR	Hendolin et al., J. Clin. Microbiol. 35:2854 (1997)
50	12	PCR	Beswick, et al., Lancet 345:386 (1999)
42	67	PCR	Hendolin, et al., Pediatr. Infect. Dis. J. 18:860 (1999)
10	49	PCR	Hendolin et al., J. Clin. Microbiol. 38:125 (2000)

[a] Number of persons in study.

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SUMMARY OF INVENTION

The present invention broadly relates to *Alloiococcus otitidis* genomic
sequence. Particularly, the invention relates to newly identified polynucleotide open
reading frames (ORFs) comprised within the genomic nucleotide sequence of
Alloiococcus otitidis, and to polypeptides encoded by the ORFs. More particularly,
the ORFs encode polypeptides that are essential for the growth and survivablity of
Alloiococcus otitidis.

Thus, in certain aspects, the invention relates to *Alloiococcus otitidis* ORFs
that encode *Alloiococcus otitidis* polypeptides that function as enzymes in various
biosynthetic pathways in the bacterium. In one embodiment, the invention relates to
a purified or isolated *Alloiococcus otitidis* nucleic acid sequence comprising a
nucleotide sequence selected from one of odd numbered sequences set forth in Seq.
ID Nos: 1 to Seq. ID Nos: 105, wherein expression of said nucleic acid is essential for
the proliferation of a cell. In a preferred embodiment the ORF selected from one of
the odd numbered sequence listings set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105
encodes an essential gene. The essential gene and the polypeptide encoded by
them include ACPS (holo-(acyl carrier protein) synthase), murF (UDP-N-
acetylmuramoylalanyl-D-glutamyl-2,6-diamino pimelate-D-alanyl-D-alanyl ligase)
murA-2 (UDP-N-acetylglucosamine 1-carboxyvinyltransferase), RpoE (DNA-directed
RNA polymerase, delta subunit), rpoA (DNA-directed RNA polymerase alpha
subunit), rpoC (RNA polymerase beta' subunit), rpoB (DNA-dependent RNA
polymerase subunit beta), dnaB/C (DNA polymerase III delta prime subunit), gyrA
(DNA gyrase A subunit), gyrB (DNA gyrase B subunit), dnaN (DNA polymerase III
beta chain, folC-2 (folyl-polyglutamate synthetase), murE (UDP-N-acetylmuramoyl-L-
alanyl-D-glutamyl-L-lysine Ligase), srtA (sortase), folC-1 (folyl-polyglutamate
synthetase), folB (dihydroneopterin aldolase), folK (7,8-dihydro-6-
hydroxymethylpterin-pyrophosphokinase), mvaS (hydroxymethylglutaryl-CoA
synthase), mvaA (3-hydroxy-3-methylglutaryl-coenzyme a reductase), murB (UDP-N-
acetylglucosaminyl-3-enolpyruvate reductase), mvaK2 (phosphomevalonate kinase),
mvaD (mevalonate diphosphate decarboxylase), mvaK1 (mevalonate kinase), coaA
(pantothenate kinase), nadE (NAD+ synthase), murI, Glutamate racemase), folP
(Dihydropteroate synthase), folA (dihydrofolate reductase), grlB (topoisomerase IV B

subunit), grlA (topoisomerase IV A subunit), rpoD (transcription initiation factor sigma), dnaG (DNA primase), era (GTP-binding protein), norA (drug-export protein), polC (DNA polymerase III, alpha subunit), obg (GTP-binding protein), yphC (similar to Escherichia coli GTP-binding protein Era), dnaE (DNA polymerase III, alpha

5   subunit), coaBC (phosphopantothenoylcysteine synthetase/decarboxylase), holA (DNA polymerase III delta subunit), coaD (phosphopantetheine adenylyltransferase) ftsZ (Cell division protein ftsZ), ftsA (Cell division protein ftsA), murG (phospho-N-acetylmuramoyl-pentapeptide-transferase), murD (UDP-N-acetylmuramoylalanine D-glutamate ligase), nadD (nicotinic acid mononucleotide adenylyltransferase), coaE

10   (dephospho-CoA kinase), murC (UDP-N-acetyl muramate-alanine ligase), fmhB FemX (factor essential for methicillin resistance), pcrA (ATP-dependent DNA helicase), murA-1 (UDP-N-acetylglucosamine 1-carboxyvinyltransferase), holB (DNA polymerase III delta' subunit) and dnaX (DNA polymerase III -gamma and tau subunits).

15   In another embodiment, the invention relates to purified or isolated nucleic acid of Alloiococcus otitidis comprising a fragment of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, wherein said fragment is selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 and more than 50 consecutive nucleotides of one of

20   one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

          In yet another embodiment, the invention relates to a purified or isolated antisense nucleic acid comprising a nucleotide sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noneoding region within an

25   operon comprising a proliferation-required gene of Alloiococcus otitidis whose activity or expression is inhibited by an antisense nucleic acid and selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

          In a nother embodiment, the invention relates to a purified or isolated nucleic acid comprising a nucleotide sequence having at least 70% identity to a nucleotide

30   sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, fragments comprising at least 25 consecutive nucleotides selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, the nucleotide sequences complementary to one of odd numbered

sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, and the sequences complementary to fragments comprising at least 25 consecutive nucleotides of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

In another embodiment, the invention relates to a vector comprising a
5   promoter operably linked to a nucleic acid encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of any one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

In another embodiment, the invention relates to purified or isolated polypeptide of Alloiococcus otitidis comprising a polypeptide whose expression is
10   inhibited by an antisense nucleic acid comprising a nucleotide sequence of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or a fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the said polypeptides.

15   In yet another embodiment, the invention relates to purified or isolated *Alloiococcus otitidis* polypeptide comprising a amino acid sequence having at least 25% amino acid identity to a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or at least 25% amino
20   acid identity to a fragment comprising at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

25   In one embodiment, the invention relates to a purified or isolated *Alloiococcus otitidis* polypeptide comprising selected from one of the even numbered sequences set forth in Seq. ID Nos: 2 to Seq. ID Nos: 106, wherein the polypeptide is essential for the proliferation of a cell..

In yet another embodiment, the invention relates to a method of producing an
30   *Alloiococcus otitidis* polypeptide comprising introducing into a cell a vector comprising a promoter operably linked to a nucleic acid comprising a nucleotide sequence encoding a polypeptide whose expression is essential for the proliferation and viability of *Alloiococcus otitidis*, and which is inhibited by an antisense nucleic

acid, and which is selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

In yet another embodiment, the invention relates to a method of inhibiting the proliferation of *Alloiococcus otitidis* in an individual comprising inhibiting the activity or reducing the amount of a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105 or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product.

In a preferred embodiment, the invention relates to method for identifying a compound which influences the activity of an *Alloiococcus otitidis* gene product , which is required for proliferation, said gene product comprising a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, said method comprising: (a) contacting said gene product with a candidate compound; and (b) determining whether said compound influences the activity of said gene product.

In a preferred embodiment, the invention relates to method for identifying a compound or an antisense nucleic acid having the ability to reduce activity or level of a *Alloiococcus otitidis* gene product, which is required for proliferation, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, said method comprising the steps of: (a) contacting a target gene or RNA encoding said gene product with a candidate compound or antisense nucleic acid; and(b) measuring the activity of said target.

In yet another preferred embodiment, the invention relates to method for inhibiting cellular proliferation of *Alloiococcus otitidis* comprising introducing an effective amount of a compound with activity against a gene whose activity or expression is essential for cellular proliferation, and which is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or a compound with activity against the product of said gene into a population of *Alloiococcus otitidis* cells expressing said gene.

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In a preferred embodiment, the invention relates to a composition comprising an effective concentration of an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1

5   to Seq. ID Nos: 105, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

. In a preferred embodiment, the invention relates to method for identifying a compound having the ability to inhibit proliferation of *Alloiococcus otitidis* cell comprising: (a) identifying a homologue of a gene or gene product whose activity or

10   level is inhibited by a nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, in a test cell, wherein said test cell is not *Alloiococcus otitidis*; (b) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homologue in said test cell; (c) contacting said test cell with a sublethal level of said inhibitory nucleic acid, thus

15   sensitizing said cell; (d) contacting the sensitized cell of step (c) with a compound; and (e) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said inhibitory nucleic acid.

In a preferred embodiment, the invention relates to a method for identifying a compound having activity against a biological pathway required for proliferation

20   comprising: (a) sensitizing a cell by providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required for proliferation, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, in said cell to

25   reduce the activity or amount of said gene product; (b) contacting the sensitized cell with a compound; and (c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

In a preferred embodiment, the invention relates to a method for identifying a

30   compound having the ability to inhibit one of the *Alloiococcus otitidis* polypeptides encoded by a polynucleotide selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, and which is essential for cellular proliferation comprising: (a) contacting a cell which expresses the polypeptide with the compound;

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and (b) determining whether said compound reduces proliferation of said contacted cell by acting on said gene product.

In a preferred embodiment, the invention relates to a method for identifying a compound having the ability to inhibit one of the purified and isolated *Alloiococcus*
5   *otitidis* polypeptides selected from one of the even numbered sequences set forth in Seq. ID No.: 2 to Seq. ID No.: 106, and which is essential for cellular proliferation comprising: (a) contacting the purified and isolated polypeptide with the compound *in vitro* in the presence or absence of a substrate, which is essential for the activity of the polypeptide; and (b) determining the effect of the compound on the polypeptide
10   by measuring the effect of the polypeptide on the substrate.

In a preferred embodiment, the invention relates to a compound which interacts with an *Alloiococcus otitidis* polypeptide selected from one of the even numbered sequences set forth in Seq. ID No.: 2 to Seq. ID No.: 106 and inhibits its activity.

15   In a preferred embodiment, the invention relates to a method for manufacturing an antimicrobial compound comprising the steps of screening one or more candidate compounds to identify a compound that reduces the activity or level of an *Alloiococcus otitidis* polypeptide selected from one of the even numbered sequences set forth in Seq. ID No.: 2 to Seq. ID No.: 106, said polypeptide
20   comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105; and manufacturing the compound so identified.

In a preferred embodiment, the invention relates to a compound which inhibits
25   proliferation of *Alloiococcus otitidis* by interacting with a gene encoding a polypeptide that is required for proliferation or with a polypeptide required for proliferation, wherein said polypeptide is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105, polypeptide encoded by a
30   nucleic acid having at least 70% nucleotide sequence identity to a nucleic acid encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105, a polypeptide having at

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least 25% amino acid identity to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105, a polypeptide encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105.

DETAILED DESCRIPTION OF THE INVENTION

A. Definitions:

By "biological pathway" is meant any discrete cell function or process that is carried out by a gene product or a subset of gene products. Biological pathways include anabolic, catabolic, enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such as cell walls. Biological pathways that are usually required for proliferation of cells or microorganisms include, but are not limited to, cell division, DNA synthesis and replication, RNA synthesis (transcription), protein synthesis (translation), protein processing, protein transport, fatty acid biosynthesis, electron transport chains, cell wall synthesis, cell membrane production, synthesis and maintenance, and the like.

By "inhibit activity of a gene or gene product" is meant having the ability to interfere with the function of a gene or gene product in such a way as to decrease expression of the gene, in such a way as to reduce the level or activity of a product of the gene or in such a way as to inhibit the interaction of the gene or gene product with other biological molecules required for its activity.

Agents which inhibit the activity of a gene include agents that inhibit transcription of the gene, agents that inhibit processing of the transcript of the gene, agents that reduce the stability of the transcript of the gene, and agents that inhibit translation of the mRNA transcribed from the gene. In microorganisms, agents which

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inhibit the activity of a gene can act to decrease expression of the operon in which the gene resides or alter the folding or processing of operon RNA so as to reduce the level or activity of the gene product. The gene product can be a non- translated RNA such as ribosomal RNA, a translated RNA (mRNA) or the protein product resulting

5   from translation of the gene mRNA. Of particular utility to the present invention are antisense RNAs that have activities against the operons or genes to which they specifically hybridze.

By "activity against a gene product" is meant having the ability to inhibit the function or to reduce the level or activity of the gene product in a cell. This includes,

10   but is not limited to, inhibiting the enzymatic activity of the gene product or the ability of the gene product to interact with other biological molecules required for its activity, including inhibiting the gene product's assembly into a multimeric structure.

By "activity against a protein" is meant having the ability to inhibit the function or to reduce the level or activity of the protein in a cell. This includes, but is not

15   limited to, inhibiting the enzymatic activity of the protein or the ability of the protein to interact with other biological molecules required for its activity, including inhibiting the protein's assembly into a multimeric structure.

By "activity against a nucleic acid" is meant having the ability to inhibit the function or to reduce the level or activity of the nucleic acid in a cell. This includes,

20   but is not limited to, inhibiting the ability of the nucleic acid interact with other biological molecules required for its activity, including inhibiting the nucleic acid's assembly into a multimeric structure.

By "activity against a gene" is meant having the ability to inhibit the function or expression of the gene in a cell. This includes, but is not limited to, inhibiting the

25   ability of the gene to interact with other biological molecules required for its activity. By "activity against an operon" is meant having the ability to inhibit the function or reduce the level of one or more products of the operon in a cell. This includes, but is not limited to, inhibiting the enzymatic activity of one or more products of the operon or the ability of one or more products of the operon to interact with other biological

30   molecules required for its activity.

By "antibiotic" is meant an agent which inhibits the proliferation of a cell or microorganism.

By "homologous coding nucleic acid" is meant a nucleic acid homologous to a nucleic acid encoding a gene product whose activity or level is inhibited by a nucleic acid selected from the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105 or a portion thereof. In some embodiments, the homologous coding nucleic acid may

5   have at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105 and fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof. In other embodiments the homologous coding nucleic acids may

10   have at least 97%, at least 5 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of the nucleotide sequences complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105 and fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof. Identity may

15   be measured using BLASTN version 2.0 with the default parameters or tBLASTX with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997)) Alternatively a "homologuous coding nucleic acid" could be identified by membership of the gene of interest to a functional orthologue cluster. All other

20   members of that orthologue cluster would be considered homologues. Such a library of functional orthologue clusters can be found at http://www.nebi.nlm.nib.gov/COG. A gene can be classified into a cluster of orthologous groups or COG by using the COGNITOR program available at the above web site, or by direct BLASTP comparison of the gene of interest to the members of the COGs and analysis of

25   these results as described by Tatusov, R.L., Galperin, M.Y., Natale, D. A. and Koonin, E.V. (2000) The COG database: a tool for genome- scale analysis of protein functions and evolution. Nucleic Acids Research v. 2 8 n. 1, pp3 3 -3 6.

The term "homologous coding nucleic acid" also includes nucleic acids comprising nucleotide sequences which encode polypeptides having at least 99%,

30   95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide comprising the amino acid sequence of one of Seq ID Nos.: 1 to Seq. ID Nos.: 105 or to a polypeptide whose expression is inhibited by a nucleic acid comprising a

nucleotide sequence of one of Seq ID Nos.: 1 to Seq. ID Nos.: 105 or fragments comprising at least 5, 10, 15, 20, 25, 30,35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.Ot78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified

5   using BLASTP with the default parameters, BLASTX with the default parameters, TBLASTN with the default parameters, or tBLASTX with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997)).

The term "homologous coding nucleic acid" also includes coding nucleic acids

10   which hybridize under stringent conditions to a nucleic acid selected from the group consisting of the nucleotide sequences complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105 and coding nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the

15   sequences complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105.

As used herein, "stringent conditions" means hybridization to filter-bound nucleic acid in 6xSSC at about 45'C followed by one or more washes in 0. lxSSC/0.2/ SDS at about 680C. Other exemplary stringent conditions may refer, e.g., to washing in 6xSSC/0.05% sodium pyrophosphate at 37C, 48'C, 55'C, and 60'C as appropriate

20   for the 5 particular probe being used.

The term "homologous coding nucleic acid" also includes coding nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleotide sequence selected from the group consisting of the sequences complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105 and coding nucleic

25   acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150,200,300,400, or 500 consecutive nucleotides of the sequences complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105. As used herein, "moderate conditions" means hybridization to filter-bound DNA in 6x sodium chloride/sodium citrate (SSC)

30   at about 45'C followed by one or more washes in 0.2xSSC/0. 1 % SDS at about 42-65'C.

The term "homologous coding nucleic acids" also includes nucleic acids comprising nucleotide sequences which encode a gene product whose activity may

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be complemented by a gene encoding a gene product whose activity is inhibited by a
nucleic acid comprising a nucleotide sequence selected from the group consisting of
Seq ID Nos.: 1 to Seq. ID Nos.: 105. In some embodiments, the homologous coding
nucleic acids may encode a gene product whose activity is complemented by the

5   gene product encoded by a nucleic acid comprising a nucleotide sequence selected
from the group consisting Seq ID Nos.: 1 to Seq. ID Nos.: 105. In other
embodiments, the homologous coding nucleic acids may comprise a nucleotide
sequence encodes a gene product whose activity is complemented by one of the
polypeptides of Seq ID Nos.: 1 to Seq. ID Nos.: 105 .

10   The term "homologous antisense nucleic acid" includes nucleic acids
comprising a nucleotide sequence having at least 97%, at least 95%, at least 90%, at
least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide
sequence selected from the group consisting of one of the sequences of Seq ID
Nos.: 1 to Seq. ID Nos.: 105 and fragments comprising at least 10, 15, 20, 25,

15   30,35,40, 50, 75, 100, 150, 200,300,400, or 500 consecutive nucleotides thereof.
Homologous antisense nucleic acids may also comprising nucleotide sequences
which have at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at
least 70% nucleotide sequence identity to a nucleotide sequence selected from the
group consisting of the sequences complementary to one of sequences of Seq ID

20   Nos.: 1 to Seq. ID Nos.: 105 and fragments comprising at least 10, 15, 20, 25, 30, 35,
40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof.
            Nucleic acid identity may be determined as described above.
The term "homologous antisense nucleic acid" also includes antisense nucleic acids
comprising nucleotide sequences which hybridize under stringent conditions to a

25   nucleotide sequence complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105
and antisense nucleic acids comprising nucleotide sequences which hybridize under
stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50,
75, 100, 150,200, 300, 400, or 500 consecutive nucleotides of the sequence
complementary to one Seq ID Nos.: 1 to Seq. ID Nos.: 105. Homologous antisense

30   nucleic acids also include antisense nucleic acids comprising nucleotide sequences
which hybridize under stringent conditions to a nucleotide sequence selected from
the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105, and antisense nucleic
acids comprising nucleotide sequences which hybridize under stringent conditions to

a fragment comprising at least 10, 15, 20,25, 30, 35, 40, 50, 75, 100,150,200,300,400, or 500 consecutive nucleotides of one of Seq ID Nos.: 1 to Seq. ID Nos.: 105.

The term "homologous antisense nucleic acid" also includes antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleotide sequence complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105 and antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of Seq ID Nos.: 1 to Seq. ID Nos.: 105. Homologous antisense nucleic acids also include antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleotide sequence selected from the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105 and antisense nucleic acids which comprising nucleotide sequences hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of one of Seq ID Nos.: 1 to Seq. ID Nos.: 105.

By "homologous polypeptide" is meant a polypeptide homologous to a polypeptide whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105 by a homologous antisense nucleic acid. The term "homologous polypeptide" includes polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide whose activity or level is inhibited by a nucleic acid selected from the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105 or by a homologous antisense nucleic acid, or polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide to a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a polypeptide whose activity or level is inhibited by a nucleic acid selected from the group consisting of Seq ID Nos.: 1 to Seq. ID Nos.: 105 or by a homologous antisense nucleic acid. Identity or similarity may be determined using the FASTA version 3. Ot78 algorithm with the default

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parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default parameters, BLASTX with the default parameters, or TBLASTN with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res.

5   25: 3389-3402 (1997).

The term homologous polypeptide also includes polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide selected from the group consisting of Seq ID Nos.: 2 to Seq. ID Nos.:

10   106 and polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 5 0, 75, 100, or 150 consecutive amino acids of a polypeptide selected from the group consisting of Seq ID Nos.: 2 to Seq. ID Nos.: 106.

15   The invention also includes polynucleotides, preferably DNA molecules, that hybridize to one of the nucleic acids of Seq ID Nos.: 2 to Seq. ID Nos.: 106 or the complements of any of the preceding nucleic acids. Such hybridization may be under stringent or moderate conditions as defined above or under other conditions which permit specific hybridization. The nucleic acid molecules of the invention that

20   hybridize to these DNA sequences include oligodeoxynucleotides ("oligos") which hybridize to the target gene under highly stringent or stringent conditions. In general, for oligos between 14 and 70 nucleotides in length the melting temperature (Tm) is calculated using the formula:

Tm ff) = 81.5 + 16.6(log[monovalent cations (molar)] + 0.41 (%.G+Q - (500N)

25   where N is the length of the probe. If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation:

Tm('C) = 81.5 + 16.6(log[monovalent cations (niolar)] + 0.4 1 (% G+C) - (0.6 1) (% formamide) - (500N) where N is the length of the probe. In general, hybridization is carried out at about 20-25 degrees below Tin (for DNA-DNA hybrids)

30   or about 10- 15 degrees below Tin (for RNA-DNA hybrids).

Other hybridization conditions are apparent to those of skill in the art (see, for example, Ausubel, F.M. et al., eds., 1989, Current Protocols in Molecular Biology,

Vol. 1, Green Publishing Associates, Inc. and John Wiley & Sons, Inc., New York, at pp. 6.3.1-6.3.6 and 2.10.3.

By "identifying a compound" is meant to screen one or more compounds in a collection of compounds such as a combinatorial chemical library or other library of

5   chemical compounds or to characterize a single compound by testing the compound in a given assay and determining whether it exhibits the desired activity.

By "inducer" is meant an agent or solution which, when placed in contact with a cell or microorganism, increases transcription, or inhibitor and/or promoter clearance/fidelity, from a desired promoter.

10   As used herein, "nucleic acid" means DNA, RNA, or modified nucleic acids. Thus, the terminology "the nucleic acid of SEQ ID NO: V or "the nucleic acid comprising the nucleotide sequence" includes both the DNA sequence of SEQ ID NO: X and an RNA sequence in which the thymidines in the DNA sequence have been substituted with uridines in the RNA sequence and in which the deoxyribose

15   backbone 'of the DNA sequence has been substituted with a ribose backbone in the RNA sequence. Modified nucleic acids are nucleic acids having nucleotides or structures which do not occur in nature, such as nucleic acids in which the internucleotide phosphate residues with methylphosphonates, phosphorothioates, phosphoramidates, and phosphate esters. Nonphosphate internucleotide analogs

20   such as siloxane bridges, carbonate bridges, thioester bridges, as well as many others known in the art may also be used in modified nucleic acids. Modified nucleic acids may also comprise, (x-anomeric nucleotide units and modified micleotides such as 1 2 dideoxy-d-ribofuranose, 1,2-dideoxy- I -phenylribofuranose, and N4, N4-ethano-5 -methyl-cytosine are contemplated for use in the present invention.

25   Modified nucleic acids may also be peptide nucleic acids in which the entire deoxyribose-phosphate backbone has been exchanged with a chemically completely different, but structurally homologous, polyamide (peptide) backbone containing 2-aminoethyl glycogen units.

As used herein, "sub-lethal" means a concentration of an agent below the

30   concentration required to inhibit all cell growth.

A proliferation-required gene or gene family is one where, in the absence or substantial reduction of a gene transcript and/or gene product, growth or viability of the cell or microorganism is reduced or eliminated. Thus, as used herein, the

terminology "proliferation- required" or "required for proliferation" encompasses instances where the absence or substantial reduction of a gene transcript and/or gene product completely eliminates cell growth as well as instances where the absence of a gene transcript and/or gene product merely reduces cell growth. These

5   proliferation-required genes can be used as potential targets for the generation of new antimicrobial agents. To achieve that goal, the present invention also encompasses assays for analyzing proliferation- required genes and for identifying compounds which interact with the gene and/or gene products of the proliferation-required genes. In addition, the present invention contemplates the expression of

10   genes and the purification of the proteins encoded by the nucleic acid sequences identified as required proliferation genes and reported herein. The purified proteins can be used to generate reagents and screen small molecule libraries or other candidate compound libraries for compounds that can be further developed to yield novel antimicrobial compounds.

15   The invention described herein addresses the need for identifying *Alloiococcus otitidis* proliferation-required gene or gene family that may be used to identify compounds, which are effective in preventing or treating most or all of the disease caused by *Alloiococcus otitidis.* The invention further addresses the need for methods of diagnosing *Alloiococcus otitidis* infection using the genes and the

20   polypeptides identified herein. The inventors have identified novel *Alloiococcus otitidis* open reading frames (Ors), which encode proteins/polypeptides that are essential for the growth and proliferation of the bacteria. More particularly, the newly identified Ors encode polypeptides that are essential for proliferation of *Alloiococcus otitidis,* and thus serve as potential targets for antimicrobial compounds. Thus, in

25   certain embodiments, the invention comprises *Alloiococcus otitidis* Ors encoding polypeptides that are essential for cellular proliferation, transcription gene products of *Alloiococcus otitidis* Ors, including, but not limited to mRNA, antisense RNA, antisense oligonucleotides, and ribozyme molecules, which can be used to inhibit or control growth of the microorganism. The invention relates also to methods of

30   detecting *Alloiococcus otitidis* nucleic acids or polypeptides and kits for diagnosing *Alloiococcus otitidis* infection. The invention also relates to pharmaceutical . compositions, in particular antimicrobial compounds in pharmaceutical compositions, for the prevention and/or treatment of bacterial infection, in particular infection

caused by or exacerbated by *Alloiococcus otitidis*.

B.   *ALLOIOCOCCUS OTITIDIS* ORF POLYNUCLEOTIDES ENCODING POLYPEPTIDES ESSENTIAL FOR PROLIFERATION

5   Isolated and purified *Alloiococcus otitidis* ORF polynucleotides of the present invention are contemplated for use in the production of *Alloiococcus otitidis* polypeptides. More specifically, in certain embodiments, the ORFs encode *Alloiococcus otitidis* polypeptides that are essential for cell proliferation. Thus, in one

10   aspect, the present invention provides isolated and purified polynucleotides (ORFs) that encode *Alloiococcus otitidis* essential for cell proliferation. In particular embodiments, a polynucleotide of the present invention is a DNA molecule, wherein the DNA may be genomic DNA, plasmid DNA or cDNA. In a preferred embodiment, a polynucleotide of the present invention is a recombinant polynucleotide, which

15   encodes an *Alloiococcus otitidis* polypeptide comprising an amino acid sequence that has at least 25% identity to an amino acid sequence of one of even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106 or a fragment thereof. In another embodiment, an isolated and purified ORF polynucleotide comprises a nucleotide sequence that has at least 70% identity to one of the ORF polynucleotide

20   nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105, a degenerate variant thereof, or a complement thereof. In yet another embodiment, an ORF polynucleotide of one of SEQ ID NO: 1 through SEQ ID NO: 105 is comprised in a plasmid vector and expressed in a host cell. In a preferred embodiment, the host cell is a prokaryotic host cell.

25   As used herein, the term "polynucleotide" means a sequence of nucleotides connected by phosphodiester linkages. Polynucleotides are presented herein in the direction from the 5' to the 3' direction. A polynucleotide of the present invention can comprise from about 10 to about several hundred thousand base pairs. Preferably, a polynucleotide comprises from about 10 to about 3,000 base pairs. Preferred lengths

30   of particular polynucleotide are set forth hereinafter.

           A polynucleotide of the present invention can be a deoxyribonucleic acid (DNA) molecule, a ribonucleic acid (RNA) molecule, or analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA. Where a

polynucleotide is a DNA molecule, that molecule can be a gene, a cDNA molecule or a genomic DNA molecule. Nucleotide bases are indicated herein by a single letter code: adenine (A), guanine (G), thymine (T) and cytosine (C).

"Isolated" means altered "by the hand of man" from the natural state. An

5   "isolated" composition or substance is one that has been changed or removed from its original environment, or both. For example, a polynucleotide or a polypeptide naturally present in a living animal is not "isolated," but the same polynucleotide or polypeptide separated from the coexisting materials of its natural state is "isolated," as the term is employed herein.

10   Preferably, an "isolated" polynucleotide is free of sequences which naturally flank the nucleic acid (*i.e.*, sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated *Alloiococcus otitidis* nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0. 5 kb or 0. 1 kb of

15   nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. However, the *Alloiococcus otitidis* nucleic acid molecule can also be fused to heterologous protein encoding or regulatory sequences and still be considered isolated.

ORF polynucleotides of the present invention may also be obtained using

20   standard cloning and screening techniques from a cDNA library derived from mRNA. Polynucleotides of the invention can also be obtained from natural sources such as genomic DNA libraries (*e.g.*, an *Alloiococcus otitidis* library) or can be synthesized using well-known and commercially available techniques. As contemplated in the present invention, ORF polynucleotides are obtained using *Alloiococcus otitidis*

25   chromosomal DNA as the template.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequences set forth in the odd numbered sequences listed in ID NO: 1 through SEQ ID NO: 105 (and fragments thereof) due to degeneracy of the genetic code, and thus encode the same *Alloiococcus otitidis* polypeptides as those encoded

30   by the amino acid sequences shown in even numbered sequences set forth in SEQ ID NO:2 through SEQ ID NO: 106

Orthologs and allelic variants of the *Alloiococcus otitidis* polynucleotides are readily identified using methods well known in the art. An allelic variant or an

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orthologue of the polynucleotides comprises a nucleotide sequence that is typically at least about 70-75%, more typically at least about 80-85%, and most typically at least about 90-95% or more homologous to the nucleotide sequence shown in one of the odd numbered sequences set forth in SEQ ID NO:1 through SEQ ID NO: 105, or a

5   fragment of these nucleotide sequences. Such nucleic acid molecules are readily identified as being able to hybridize, preferably under stringent conditions, to the nucleotide sequence shown in one of the odd numbered sequences set forth in SEQ ID NO:1 through SEQ ID NO: 105, or a fragment of these nucleotide sequences.

Moreover, the polynucleotides of the invention can comprise only a fragment

10 of the coding region of an *Alloiococcus otitidis* polynucleotide or gene, such as a fragment of one of the odd numbered sequences set forth in SEQ ID NO:1 through SEQ ID NO: 105.

When the ORF polynucleotides of the invention are used for the recombinant production of *Alloiococcus otitidis* polypeptides of the present invention, the

15 polynucleotide may include the coding sequence for the mature polypeptide, by itself, or the coding sequence for the mature polypeptide in reading frame with other coding sequences, such as those encoding a leader or secretory sequence, a pre-, or pro- or prepro- protein sequence, or other fusion peptide portions. For example, a marker sequence which facilitates purification of the fused polypeptide can be linked to the

20 coding sequence (*see* Gentz *et al.*, 1989, incorporated herein by reference). Thus, contemplated in the present invention is the preparation of polynucleotides encoding fusion polypeptides permitting His-tag purification of expression products. The polynucleotide may also contain non-coding 5' and 3' sequences, such as transcribed, non-translated sequences, splicing and polyadenylation signals.

25   Thus, a polynucleotide encoding a polypeptide of the present invention, including homologs and orthologs from species other than *Alloiococcus otitidis*, may be obtained by a process which comprises the steps of screening an appropriate library under stringent hybridization conditions with a labeled probe having the sequence of one of the odd numbered sequences set forth in SEQ ID NO:1 through

30 SEQ ID NO: 105 or a fragment thereof; and isolating full-length cDNA and genomic clones containing the polynucleotide sequence. Such hybridization techniques are well known to the skilled artisan. The skilled artisan will appreciate that, in many cases, an isolated cDNA sequence will be incomplete, in that the region coding for

the polypeptide is cut short at the 5' end of the cDNA. This is a consequence of reverse transcriptase, an enzyme with inherently low "processivity" (a measure of the ability of the enzyme to remain attached to the template during the polymerization reaction), failing to complete a DNA copy of the mRNA template during the first-

5   strand cDNA synthesis.

Thus, in certain embodiments, the polynucleotide sequence information provided by the present invention allows for the preparation of relatively short DNA (or RNA) oligonucleotide sequences having the ability to specifically hybridize to gene sequences of the selected polynucleotides disclosed herein. The term

10   "oligonucleotide" as used herein is defined as a molecule comprised of two or more deoxyribonucleotides or ribonucleotides, usually more than three (3), and typically more than ten (10) and up to one hundred (100) or more (although preferably between twenty and thirty). The exact size will depend on many factors, which in turn depends on the ultimate function or use of the oligonucleotide. Thus, in

15   particular embodiments of the invention, nucleic acid probes of an appropriate length are prepared based on a consideration of a selected nucleotide sequence, e.g., a sequence such as that shown in one of the odd numbered sequences set forth in SEQ ID NO:1 through SEQ ID NO: 105. The ability of such nucleic acid probes to specifically hybridize to a polynucleotide encoding an *Alloiococcus otitidis*

20   polypeptide lends them particular utility in a variety of embodiments. Most importantly, the probes can be used in a variety of assays for detecting the presence of complementary sequences in a given sample.

In certain embodiments, it is advantageous to use oligonucleotide primers. These primers are generated in any manner, including chemical synthesis, DNA

25   replication, reverse transcription, or a combination thereof. The sequence of such primers is designed using a polynucleotide of the present invention for use in detecting, amplifying or mutating a defined segment of an ORF polynucleotide that encodes an *Alloiococcus otitidis* polypeptide from prokaryotic cells using polymerase chain reaction (PCR) technology.

30   In certain embodiments, it is advantageous to employ a polynucleotide of the present invention in combination with an appropriate label for detecting hybrid formation. A wide variety of appropriate labels are known in the art, including

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radioactive, enzymatic or other ligands, such as avidin/biotin, which are capable of giving a detectable signal.

Polynucleotides which are identical or sufficiently identical to a nucleotide sequence contained in one of the odd numbered sequences set forth in SEQ ID
5   NO:1 through SEQ ID NO: 105, or a fragment thereof, may be used as hybridization probes for cDNA and genomic DNA or as primers for a nucleic acid amplification (PCR) reaction, to isolate full-length cDNAs and genomic clones encoding polypeptides of the present invention and to isolate cDNA and genomic clones of other genes (including genes encoding homologs and orthologs from species other
10 than Alloiococcus otitidis) that have a high sequence similarity to polynucleotide sequences set forth in one of the odd numbered sequences set forth in SEQ ID NO:1 through SEQ ID NO:105, or a fragment thereof. Typically these nucleotide sequences are from at least 70% identical to at least about 95% identical to that of the reference polynucleotide sequence. The probes or primers will generally
15 comprise at least 15 nucleotides, preferably, at least 30 nucleotides and may have at least 50 nucleotides. Particularly preferred probes will have between 30 and 50 nucleotides.

There are several methods available and well known to those skilled in the art to obtain full-length cDNAs, or extend short cDNAs, for example those based on the
20 method of Rapid Amplification of cDNA ends (RACE) (see, Frohman et al., 1988). Recent modifications of the technique, exemplified by the Marathon™ technology [Promega, Madison, WI], for example, have significantly simplified the search for longer cDNAs. In the Marathon™ technology, cDNAs have been prepared from mRNA extracted from a chosen tissue and an "adaptor" sequence ligated onto each
25 end. Nucleic acid amplification (PCR) is then carried out to amplify the "missing" 5′ end of the cDNA using a combination of gene specific and adaptor specific oligonucleotide primers. The PCR reaction is then repeated using "nested" primers, that is, primers designed to anneal within the amplified product (typically an adaptor specific primer that anneals further 3' in the adaptor sequence and a gene specific
30 primer that anneals further 5' in the known gene sequence). The products of this reaction are then analyzed by DNA sequencing and a full-length cDNA constructed either by joining the product directly to the existing cDNA to give a complete

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sequence, or carrying out a separate full-length PCR using the new sequence information for the design of the 5' primer.

To provide certain of the advantages in accordance with the present invention, a preferred nucleic acid sequence employed for hybridization studies or

5   assays includes probe molecules that are complementary to at least a 10 to about 70 nucleotides long stretch of a polynucleotide that encodes an *Alloiococcus otitidis* polypeptide, such as that shown in one of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106. A size of at least 10 nucleotides in length helps to ensure that the fragment will be of sufficient length to form a duplex

10   molecule that is both stable and selective. Molecules having complementary sequences over stretches greater than 10 bases in length are generally preferred in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. It is generally preferable to design nucleic acid molecules with gene-complementary stretches of 25 to 40

15   nucleotides, 55 to 70 nucleotides, or even longer where desired. For example, such fragments are readily prepared by directly synthesizing the fragment by chemical means, by application of nucleic acid reproduction technology, such as the PCR technology (U.S. Patent 4,683,202, incorporated herein by reference), or by excising selected DNA fragments from recombinant plasmids containing appropriate inserts

20   and suitable restriction enzyme sites.

In another aspect, the present invention contemplates an isolated and purified polynucleotide comprising a nucleotide sequence that is identical or complementary to a segment of at least 10 contiguous bases of one of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105, wherein the polynucleotide

25   hybridizes to a polynucleotide that encodes an *Alloiococcus otitidis* polypeptide. Preferably, the isolated and purified polynucleotide comprises a base sequence that is identical or complementary to a segment of at least 25 to 70 contiguous bases of one of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105. For example, the polynucleotide of the invention can comprise a segment of

30   bases identical or complementary to from 40 to 55 contiguous bases of the disclosed nucleotide sequences.

Accordingly, a polynucleotide probe molecule of the invention can be used for its ability to selectively form duplex molecules with complementary stretches of the

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gene. Depending on the application envisioned, varying conditions of hybridization are employed to achieve varying degrees of selectivity of the probe toward the target sequence. For applications requiring a high degree of selectivity, relatively stringent conditions are employed to form the hybrids. Of course, for some applications, for
5   example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template or where one seeks to isolate an *Alloiococcus otitidis* homologous polypeptide coding sequence from other cells, functional equivalents, or the like, less stringent hybridization conditions are typically needed to allow formation of the heteroduplex (see Table 2). Cross-hybridizing species are
10   thereby readily identified as positively hybridizing signals with respect to control hybridizations. Thus, hybridization conditions are readily manipulated, and thus will generally be a method of choice depending on the desired results.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template or
15   where one seeks to isolate a homologous polypeptide coding sequence from other cells, functional equivalents, or the like, less stringent hybridization conditions are typically needed to allow formation of the heteroduplex. Cross-hybridizing species are thereby readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be
20   rendered more stringent by the addition of increasing amounts of formamide, which serves to destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions are readily manipulated, and thus are generally a method of choice depending on the desired results.

The present invention also includes polynucleotides capable of hybridizing
25   under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced
30   stringency conditions are at least as stringent as, for example, conditions M-R.

TABLE 2

STRINGENCY CONDITIONS

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp)[I]	Hybridization Temperature and Buffer[H]	Wash Temperature and Buffer[H]
A	DNA:DNA	> 50	65°C; 1xSSC -or- 42°C; 1xSSC, 50% formamide	65°C; 0.3xSSC
B	DNA:DNA	< 50	T_B; 1xSSC	T_B; 1xSSC
C	DNA:RNA	> 50	67°C; 1xSSC -or- 45°C; 1xSSC, 50% formamide	67°C; 0.3xSSC
D	DNA:RNA	< 50	T_D; 1xSSC	T_D; 1xSSC
E	RNA:RNA	> 50	70°C; 1xSSC -or- 50°C; 1xSSC, 50% formamide	70°C; 0.3xSSC
F	RNA:RNA	< 50	T_F; 1xSSC	T_F; 1xSSC
G	DNA:DNA	> 50	65°C; 4xSSC -or- 42°C; 4xSSC, 50% formamide	65°C; 1xSSC
H	DNA:DNA	< 50	T_H; 4xSSC	T_H; 4xSSC
I	DNA:RNA	> 50	67°C; 4xSSC -or- 45°C; 4xSSC, 50% formamide	67°C; 1xSSC
J	DNA:RNA	< 50	T_J; 4xSSC	T_J; 4xSSC
K	RNA:RNA	> 50	70°C; 4xSSC -or- 50EC; 4xSSC, 50% formamide	67°C; 1xSSC
L	RNA:RNA	< 50	T_L; 2xSSC	T_L; 2xSSC
M	DNA:DNA	> 50	50°C; 4xSSC -or- 40°C; 6xSSC, 50% formamide	50°C; 2xSSC
N	DNA:DNA	< 50	T_N; 6xSSC	T_N; 6xSSC
O	DNA:RNA	> 50	55°C; 4xSSC -or- 42°C; 6xSSC, 50% formamide	55°C; 2xSSC
P	DNA:RNA	< 50	T_P; 6xSSC	T_P; 6xSSC
Q	RNA:RNA	> 50	60°C; 4xSSC -or- 45°C; 6xSSC, 50% formamide	60°C; 2xSSC
R	RNA:RNA	< 50	T_R; 4xSSC	T_R; 4xSSC

(bp)[I]: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target

polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence

5   complementarity.

Buffer^H: SSPE (1xSSPE is 0.15M NaCl, 10mM NaH$_2$PO$_4$, and 1.25mM EDTA, pH 7.4), can be substituted for SSC (1xSSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

10   T$_B$ through T$_R$: The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10EC less than the melting temperature (T$_m$) of the hybrid, where T$_m$ is determined according to the following equations. For hybrids less than 18 base pairs in length, T$_m$(EC) = 2(# of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T$_m$(EC) = 81.5 +

15   16.6(log$_{10}$[Na$^+$]) + 0.41(%G+C) - (600/N), where N is the number of bases in the hybrid, and [Na$^+$] is the concentration of sodium ions in the hybridization buffer ([Na$^+$] for 1xSSC = 0.165 M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook *et al.*, 1989, Molecular Cloning: A Laboratory Manual, Cold

20   Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Ausubel *et al.*, 1995, Current Protocols in Molecular Biology, Eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

In addition to the nucleic acid molecules encoding *Alloiococcus otitidis* polypeptides described above, another aspect of the invention pertains to isolated

25   nucleic acid molecules that are antisense thereto. An "antisense" nucleic acid comprises a nucleotide sequence that is complementary to a "sense" nucleic acid encoding a protein, *e.g.*, complementary to the coding strand of a double-stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid

30   can be complementary to an entire *Alloiococcus otitidis* coding strand, or to only a fragment thereof. In one embodiment, an antisense nucleic acid molecule is antisense to a "coding region" of the coding strand of a nucleotide sequence encoding an *Alloiococcus otitidis* polypeptide.

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The term "coding region" refers to the region of the nucleotide sequence comprising codons which are translated into amino acid residues, *e.g.*, the entire coding region of each of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105. In another embodiment, the antisense nucleic acid

5   molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding an *Alloiococcus otitidis* polypeptide. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into amino acids (*i.e.*, also referred to as 5' and 3' untranslated regions).

Given the coding strand sequence encoding the *Alloiococcus otitidis*

10   polypeptides disclosed herein antisense nucleic acids of the invention can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of *Alloiococcus otitidis* mRNA, but more preferably is an oligonucleotide which is antisense to only a fragment of the coding or noncoding region of *Alloiococcus otitidis*

15   mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of *Alloiococcus otitidis* mRNA.

An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using

20   procedures known in the art. For example, an antisense nucleic acid (*e.g.*, an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, *e.g.*, phosphorothioate derivatives

25   and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine,

30   N6-isopentenyladenine, I-methylguanine, I-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-

methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-

5   diaminopurine.

Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (*i.e.*, RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the

10   following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding an *Alloiococcus otitidis* polypeptide to thereby inhibit expression of the polypeptide, *e.g.*, by inhibiting transcription and/or

15   translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of an antisense nucleic acid molecule of the invention includes direct injection at a tissue site.

20   Alternatively, an antisense nucleic acid molecule can be modified to target selected cells and then administered systemically. For example, for systemic administration, an antisense molecule can be modified such that it specifically binds to a receptor or an antigen expressed on a selected cell surface, *e.g.*, by linking the antisense nucleic acid molecule to a peptide or an antibody which binds to a cell surface receptor or

25   antigen. The antisense nucleic acid molecule can also be delivered to cells using the vectors described herein.

In yet another embodiment, the antisense nucleic acid molecule of the invention is an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which,

30   contrary to the usual γ-units, the strands run parallel to each other (Gaultier *et al.*, 1987). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue *et al.*, 1987) or a chimeric RNA-DNA analogue (Inoue *et al.*, 1987).

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In still another embodiment, an antisense nucleic acid of the invention is a
ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity that are
capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they
have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes
5   described in Haselhoff and Gerlach, 1988) can be used to catalytically cleave
Alloiococcus otitidis mRNA transcripts to thereby inhibit translation of Alloiococcus
otitidis mRNA. A ribozyme having specificity for an Alloiococcus otitidis-encoding
nucleic acid can be designed based upon the nucleotide sequence of an
Alloiococcus otitidis cDNA disclosed herein. For example, a derivative of a
10   Tetrahymena L-19 IVS RNA can be constructed in which the nucleotide sequence of
the active site is complementary to the nucleotide sequence to be cleaved in an
Alloiococcus otitidis-encoding mRNA. See, e.g., Cech et al. U.S. 4,987,071 and
Cech et al. U.S. 5,116,742 both incorporated herein in their entirety by reference.
Alternatively, Alloiococcus otitidis mRNA can be used to select a catalytic RNA
15   having a specific ribonuclease activity from a pool of RNA molecules. See, e.g.,
Bartel and Szostak, 1993.

Alternatively Alloiococcus otitidis gene expression can be inhibited by
targeting nucleotide sequences complementary to the regulatory region of the
Alloiococcus otitidis gene (e.g., the Alloiococcus otitidis gene promoter and/or
20   enhancers) to form triple helical structures that prevent transcription of the
Alloiococcus otitidis gene in target cells. See generally, Helene, 1991; Helene et al.,
1992; and Maher, 1992.

Alloiococcus otitidis gene expression can also be inhibited using RNA
interference (RNAi). This is a technique for post-transcriptional gene silencing
25·   (PTGS), in which target gene activity is specifically abolished with cognate double-
stranded RNA (dsRNA). RNAi resembles in many aspects PTGS in plants and has
been detected in many invertebrates including trypanosome, hydra, planaria,
nematode and fruit fly (Drosophila melangnoster). It may be involved in the
modulation of transposable element mobilization and antiviral state formation. RNAi
30   in mammalian systems is disclosed in WO 00/63364, which is incorporated by
reference herein in its entirety. Basically, dsRNA of at least about 600 nucleotides,
homologous to the target is introduced into the cell and a sequence specific reduction
in gene activity is observed.

C.   *ALLOIOCOCCUS OTITIDIS* POLYPEPTIDES

5   In particular embodiments, the present invention provides isolated and
purified *Alloiococcus otitidis* polypeptides. Preferably, an *Alloiococcus otitidis*
polypeptide of the invention is a recombinant polypeptide. In certain embodiments,
an *Alloiococcus otitidis* polypeptide of the present invention comprises the amino acid
sequence that has at least 25% identity to the amino acid sequence of one of the
even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106, a
10   biological equivalent thereof, or a fragment thereof.

         An *Alloiococcus otitidis* polypeptide according to the present invention
encompasses a polypeptide that comprises: 1) the amino acid sequence shown in
one of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO:
106) functional and non-functional naturally occurring variants or biological
15   equivalents of *Alloiococcus otitidis* polypeptides of the even numbered sequences set
forth in SEQ ID NO: 2 through SEQ ID NO: 106 and recombinantly produced variants
or biological equivalents of *Alloiococcus otitidis* polypeptides set out in SEQ ID NO: 2
through SEQ ID NO: 106) polypeptides isolated from organisms other than
Alloiococcus otitidis (orthologs of *Alloiococcus otitidis* polypeptides.)

20   A biological equivalent or variant of an *Alloiococcus otitidis* polypeptide
according to the present invention encompasses 1) a polypeptide isolated from
Alloiococcus otitidis; and 2) a polypeptide that contains substantial homology to an
Alloiococcus otitidis polypeptide.

         Biological equivalents or variants of *Alloiococcus otitidis* include both
25   functional and non-functional *Alloiococcus otitidis* polypeptides. Functional biological
equivalents or variants are naturally occurring amino acid sequence variants of an
Alloiococcus otitidis polypeptide that maintain the ability to elicit an immunological or
antigenic response in a subject. Functional variants will typically contain only
conservative substitutions of one or more amino acids in any one of even numbered
30   sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106 or substitution,
deletion or insertion of non-critical residues in non-critical regions of the polypeptide.

         The present invention further provides non-*Alloiococcus otitidis* orthologues of
Alloiococcus otitidis polypeptides. Orthologues of *Alloiococcus otitidis* polypeptides

are polypeptides that are isolated from non-*Alloiococcus otitidis* organisms and possess antigenic capabilities of the *Alloiococcus otitidis* polypeptide. Orthologues of an *Alloiococcus otitidis* polypeptide can readily be identified as comprising an amino acid sequence that is substantially homologous to one of the even numbered

5   sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106.

Modifications and changes can be made in the structure of a polypeptide of the present invention and still obtain a molecule having *Alloiococcus otitidis* antigenicity. For example, certain amino acids can be substituted for other amino acids in a sequence without appreciable loss of antigenicity. Because it is the

10   interactive capacity and nature of a polypeptide that defines that polypeptide's biological functional activity, certain amino acid sequence substitutions can be made in a polypeptide sequence (or, of course, its underlying DNA coding sequence) and nevertheless obtain a polypeptide with like properties.

In making such changes, the hydropathic index of amino acids can be

15   considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a polypeptide is generally understood in the art (Kyte & Doolittle, 1982). It is known that certain amino acids can be substituted for other amino acids having a similar hydropathic index or score and still result in a polypeptide with similar biological activity. Each amino acid has been assigned a

20   hydropathic index on the basis of its hydrophobicity and charge characteristics. Those indices are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5);

25   lysine (-3.9); and arginine (-4.5).

It is believed that the relative hydropathic character of the amino acid residue determines the secondary and tertiary structure of the resultant polypeptide, which in turn defines the interaction of the polypeptide with other molecules, such as enzymes, substrates, receptors, antibodies, antigens, and the like. It is known in the

30   art that an amino acid can be substituted by another amino acid having a similar hydropathic index and still obtain a functionally equivalent polypeptide. In such changes, the substitution of amino acids whose hydropathic indices are within +/-2 is

preferred, those within +/-1 are particularly preferred, and those within +/-0.5 are even more particularly preferred.

Substitution of like amino acids can also be made on the basis of hydrophilicity, particularly where the biologically functional equivalent polypeptide or peptide thereby created is intended for use in immunological embodiments. U.S. Pat. No. 4,554,101, incorporated herein by reference, states that the greatest local average hydrophilicity of a polypeptide, as governed by the hydrophilicity of its adjacent amino acids, correlates with its immunogenicity and antigenicity, i.e. with a biological property of the polypeptide.

As detailed in U.S. Pat. No. 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 ±1); glutamate (+3.0 ±1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); proline (-0.5 ±1); threonine (-0.4); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5); tryptophan (-3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent polypeptide. In such changes, the substitution of amino acids whose hydrophilicity values are within ±2 is preferred, those which are within ±1 are particularly preferred, and those within ±0.5 are even more particularly preferred.

As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions which take various of the foregoing characteristics into consideration are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine (See Table 3, below). The present invention thus contemplates functional or biological equivalents of an Alloiococcus otitidis polypeptide as set forth above.

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TABLE 3:
AMINO ACID SUBSTITUTIONS

Original Residue	Exemplary Residue Substitution
Ala	Gly; Ser
Arg	Lys
Asn	Gln; His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Ala
His	Asn; Gln
Ile	Leu; Val
Leu	Ile; Val
Lys	Arg
Met	Met; Leu; Tyr
Ser	Thr
Thr	Ser
Trp	Tyr
Tyr	Trp; Phe
Val	Ile; Leu

Biological or functional equivalents of a polypeptide are also prepared using

5   site-specific mutagenesis. Site-specific mutagenesis is a technique useful in the

preparation of second generation polypeptides, or biologically functional equivalent

polypeptides or peptides, derived from the sequences thereof, through specific

mutagenesis of the underlying DNA. As noted above, such changes can be

desirable where amino acid substitutions are desirable. The technique further

10   provides a capacity to prepare and test sequence variants, for example, incorporating

one or more of the foregoing considerations, by introducing one or more nucleotide

sequence changes into the DNA. Site-specific mutagenesis allows the production of

mutants through the use of specific oligonucleotide sequences which encode the

DNA sequence of the desired mutation, as well as a sufficient number of adjacent

15   nucleotides, to provide a primer sequence of sufficient size and sequence complexity

to form a stable duplex on both sides of the deletion junction being traversed.

Typically, a primer of about 17 to 25 nucleotides in length is preferred, with about 5 to

10 residues on both sides of the site of the alteration of the sequence.

In general, the technique of site-specific mutagenesis is well known in the art.

20   As will be appreciated, the technique typically employs a phage vector, that can exist

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in both a single stranded and double stranded form. Typically, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector which includes within its sequence a DNA sequence which encodes all or a portion of the *Alloiococcus otitidis* polypeptide sequence selected. An

5   oligonucleotide primer bearing the desired mutated sequence is prepared (*e.g.*, synthetically). This primer is then annealed to the singled-stranded vector, and extended by the use of enzymes such as *Escherichia coli* polymerase I Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated

10 sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells such as *Escherichia coli* cells and clones are selected which include recombinant vectors bearing the mutation. Commercially available kits come with all the reagents necessary, except the oligonucleotide primers.

15   An *Alloiococcus otitidis* polypeptide or polypeptide antigen of the present invention is understood to be any *Alloiococcus otitidis* polypeptide comprising substantial sequence similarity, structural similarity and/or functional similarity to an *Alloiococcus otitidis* polypeptide comprising the amino acid sequence of one of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106. In

20 addition, an *Alloiococcus otitidis* polypeptide or polypeptide antigen of the invention is not limited to a particular source. Thus, the invention provides for the general detection and isolation of the polypeptides from a variety of sources.

     It is contemplated in the present invention, that an *Alloiococcus otitidis* polypeptide may advantageously be cleaved into fragments for use in further

25 structural or functional analysis, or in the generation of reagents such as *Alloiococcus otitidis*-related polypeptides and *Alloiococcus otitidis*-specific antibodies. This can be accomplished by treating purified or unpurified *Alloiococcus otitidis* polypeptides with a peptidase such as endoproteinase glu-C (Boehringer, Indianapolis, IN). Treatment with CNBr is another method by which peptide fragments may be produced from

30 natural *Alloiococcus otitidis* polypeptides. Recombinant techniques also can be used to produce specific fragments of an *Alloiococcus otitidis* polypeptide.

     In addition, the inventors also contemplate that compounds sterically similar to a particular *Alloiococcus otitidis* polypeptide antigen, called peptidomimetics, may

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be formulated to mimic the key portions of the peptide structure. Peptidemimetics are peptide-containing molecules that mimic elements of protein secondary structure. (*See,* for example, Johnson *et al.,* 1993.) The underlying rationale behind the use of peptide mimetics is that the peptide backbone of proteins exists chiefly to orient

5   amino acid side chains in such a way as to facilitate molecular interactions, such as those of receptor and ligand.

Successful applications of the peptide mimetic concept have thus far focused on mimetics of β-turns within proteins. Likely β-turn structures, within *Alloiococcus otitidis,* can be predicted by computer-based algorithms as discussed above. Once

10   the component amino acids of the turn are determined, mimetics can be constructed to achieve a similar spatial orientation of the essential elements of the amino acid side chains, as discussed in Johnson *et al.,* 1993.

Fragments of the *Alloiococcus otitidis* polypeptides are also included in the invention. A fragment is a polypeptide having an amino acid sequence that entirely is

15   the same as a part, but not all, of the amino acid sequence. The fragment can comprise, for example, at least 7 or more (e.g., 8, 10 12, 14, 16, 18, 20 or more) contiguous amino acids of an one of amino acid sequence selected from one of the even numbered sequences set forth in SEQ ID NO.: 2 through SEQ ID NO.: 106. Fragments may be "freestanding" or comprised within a larger polypeptide of which

20   they form a part or region, most preferably as a single, continuous region. In one embodiment, the fragments include at least one epitope of the mature polypeptide sequence.

"Fusion protein" refers to a protein encoded by two, often unrelated, fused genes or fragments thereof. For example, fusion proteins comprising various

25   portions of constant region of immunoglobulin molecules together with another human protein or part thereof have been described. In many cases, employing an immunoglobulin Fc region as a part of a fusion protein is advantageous for use in therapy and diagnosis resulting in, for example, improved pharmacokinetic properties (*see, e.g.,* EP-A 0232 2621). On the other hand, for some uses it would be desirable

30   to be able to delete the Fc part after the fusion protein has been expressed, detected and purified.

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D. ALLOIOCOCCUS OTITIDIS POLYNUCLEOTIDE AND POLYPEPTIDE VARIANTS

"Variant" as the term is used herein, is a polynucleotide or polypeptide that differs from a reference polynucleotide or polypeptide respectively, but retains

5   essential properties. A typical variant of a polynucleotide differs in nucleotide sequence from another, reference polynucleotide. Changes in the nucleotide sequence of the variant may or may not alter the amino acid sequence of a polypeptide encoded by the reference polynucleotide. Nucleotide changes may result in amino acid substitutions, additions, deletions, fusions and truncations in the

10   polypeptide encoded by the reference sequence, as discussed below. A typical variant of a polypeptide differs in amino acid sequence from another, reference polypeptide. Generally, differences are limited so that the sequences of the reference polypeptide and the variant are closely similar overall and, in many regions, identical. A variant and reference polypeptide may differ in amino acid

15   sequence by one or more substitutions, additions and deletions in any combination. A substituted or inserted amino acid residue may or may not be one encoded by the genetic code. A variant of a polynucleotide or polypeptide may be a naturally occurring variant such as an allelic variant, or it may be a variant that is not known to occur naturally. Non-naturally occurring variants of polynucleotides and polypeptides

20   may be made by mutagenesis techniques or by direct synthesis.

"Identity," as known in the art, is a relationship between two or more polypeptide sequences or two or more polynucleotide sequences, as determined by comparing the sequences. In the art, "identity" also means the degree of sequence relatedness between polypeptide or polynucleotide sequences, as the case may be,

25   as determined by the match between strings of such sequences. "Identity" can be readily calculated by known methods, including but not limited to those described in (Computational Molecular Biology, Lesk, A. M., ed., Oxford University Press, New York, 1988; Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part I,

30   Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991; and Carillo, H., and Lipman, D., SIAM J. Applied Math., 48: 1073 (1988). Preferred methods to determine identity are designed to give the largest match

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between the sequences tested. Methods to determine identity are codified in publicly available computer programs. Preferred computer program methods to determine identity between two sequences include, but are not limited to, the GCG program package (Devereux, J., *et al* 1984), BLASTP, BLASTN, and FASTA (Altschul, S. F.,

5   *et al.*, 1990. The BLASTX program is publicly available from NCBI and other sources (BLAST Manual, Altschul, S., *et al.*, NCBI NLM NIH Bethesda, Md. 20894; Altschul, S., *et al.*, 1990). The well known Smith-Waterman algorithm may also be used to determine identity.

           By way of example, a polynucleotide sequence of the present invention may

10   be identical to the reference sequence of one of SEQ ID NO:1 through SEQ ID NO: 105, that is be 100% identical, or it may include up to a certain integer number of nucleotide alterations as compared to the reference sequence. Such alterations are selected from the group consisting of at least one nucleotide deletion, substitution, including transition and transversion, or insertion, and wherein said alterations may

15   occur at the 5' or 3' terminal positions of the reference nucleotide sequence or anywhere between those terminal positions, interspersed either individually among the nucleotides in the reference sequence or in one or more contiguous groups within the reference sequence. The number of nucleotide alterations is determined by multiplying the total number of nucleotides in one of the odd numbered sequences

20   set forth in SEQ ID NO: 1 through SEQ ID NO: 105 by the numerical percent of the respective percent identity (divided by 100) and subtracting that product from said total number of nucleotides in one of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105.

           For example, the alterations in an isolated *Alloiococcus otitidis* polynucleotide

25   comprise a polynucleotide sequence that has at least 70% identity to the nucleic acid sequence of one of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105; a degenerate variant thereof or a fragment thereof, wherein the polynucleotide sequence may include up to n_n nucleic acid alterations over the entire polynucleotide region of the nucleic acid sequence of any on of the odd numbered

30   sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105, wherein n_n is the maximum number of alterations and is calculated by the formula:

$$n_n \leq x_n - (x_n \cdot y),$$

in which x_n is the total number of nucleic acids of one of SEQ ID NO:1 through SEQ ID NO:105 and y has a value of 0.70, wherein any non-integer product of x_n and y is rounded down to the nearest integer prior to subtracting such product from x_n. Of course, y may also have a value of 0.80 for 80%, 0.85 for 85%, 0.90 for 90% 0.95 for
5   95%, etc.

Similarly, a polypeptide sequence of the present invention may be identical to the reference sequence of any one of even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106, that is 100% identical, or it may include up to a certain integer number of amino acid alterations as compared to the reference
10   sequence such that the percentage identity is less than 100%. Such alterations are selected from the group consisting of at least one amino acid deletion, substitution, including conservative and non-conservative substitution, or insertion, and wherein said alterations may occur at the amino- or carboxy-terminal positions of the reference polypeptide sequence or anywhere between those terminal positions,
15   interspersed either individually among the amino acids in the reference sequence or in one or more contiguous groups within the reference sequence. The number of amino acid alterations for a given % identity is determined by multiplying the total number of amino acids in one of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106 by the numerical percent of the respective percent
20   identity (divided by 100) and then subtracting that product from said total number of amino acids in one of the even numbered sequences set forth in SEQ ID NO: 2 · through SEQ ID NO: 106, or:

$$n_a \leq x_a - (x_a \bullet y),$$

wherein n_a is the number of amino acid alterations, x_a is the total number of amino
25   acids in one of SEQ ID NO: 2 through SEQ ID NO: 106, and y is, for instance 0.70 for 70%, 0.80 for 80%, 0.85 for 85% etc., and wherein any non-integer product of ·x.sub.a and y is rounded down to the nearest integer prior to subtracting it from x_a.

E.   VECTORS, HOST CELLS AND RECOMBINANT *ALLOIOCOCCUS OTITIDIS*
30   POLYPEPTIDES

In a preferred embodiment, the present invention provides expression vectors comprising ORF polynucleotides that encode *Alloiococcus otitidis* polypeptides. Preferably, the expression vectors of the present invention comprise ORF

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polynucleotides that encode *Alloiococcus otitidis* polypeptides comprising the amino acid residue sequence of one of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106. More preferably, the expression vectors of the present invention comprise a polynucleotide comprising the nucleotide base sequence of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105. Even more preferably, the expression vectors of the invention comprise a polynucleotide operatively linked to promoter. Still more preferably, the expression vectors of the invention comprise a polynucleotide operatively linked to a prokaryotic promoter. Alternatively, the expression vectors of the present invention comprise a polynucleotide operatively linked to an enhancer-promoter, that is, an eukaryotic promoter. The expression vectors further comprise a polyadenylation signal that is positioned 3' of the carboxy-terminal amino acid and within a transcriptional unit of the encoded polypeptide.

Expression of proteins in prokaryotes is most often carried out in *Escherichia coli* with vectors containing constitutive or inducible promoters directing the expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase.

Typical fusion expression vectors include pGEX (Pharmacia Biotech Inc; Smith and Johnson, 1988), pMAL (New England Biolabs, Beverly; MA) and pRIT5 (Pharmacia, Piscataway, NJ) which fuse glutathione S- transferase (GST), maltose E binding protein, or protein A, respectively, to the target recombinant protein.

In one embodiment, the coding sequence of the *Alloiococcus otitidis* polynucleotide is cloned into a pGEX expression vector to create a vector encoding a fusion protein comprising, from the N-terminus to the C-terminus, GST-thrombin cleavage site-*Alloiococcus otitidis* polypeptide. The fusion protein can be purified by

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affinity chromatography using glutathione-agarose resin. Recombinant *Alloiococcus otitidis* polypeptide unfused to GST can be recovered by cleavage of the fusion protein with thrombin.

Examples of suitable inducible non-fusion *Escherichia coli* expression vectors
5 include pTrc (Amann *et al.*, 1988) and pET I I d (Studier *et al.*, 1990). Target gene expression from the pTrc vector relies on host RNA polymerase transcription from a hybrid trp-lac fusion promoter. Target gene expression from the pET I I d vector relies on transcription from a T7 gn1 0-lac fusion promoter mediated by a coexpressed viral RNA polymerase T7 gnl. This viral polymerase is supplied by host
10 strains BL21 (DE3) or HMS I 74(DE3) from a resident prophage harboring a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

One strategy to maximize recombinant protein expression in *Escherichia coli* is to express the protein in a host bacterium with an impaired capacity to proteolytically cleave the recombinant protein. Another strategy is to alter the nucleic
15 acid sequence of the nucleic acid to be inserted into an expression vector so that the individual codons for each amino acid are those preferentially utilized in *Escherichia coli*. Such alteration of nucleic acid sequences of the invention can be carried out by standard DNA mutagenesis or synthesis techniques.

In another embodiment, the *Alloiococcus otitidis* polynucleotide expression
20 vector is a yeast expression vector. Examples of vectors for expression in a yeast such as *S. cerevisiae* include pYepSec I (Baldari, *et al.*, 1987), pMFa (Kurjan and Herskowitz, 1982), pJRY88 (Schultz *et al.*, 1987), and pYES2 (Invitrogen Corporation, San Diego, CA).

Alternatively, an *Alloiococcus otitidis* polynucleotide is expressed in insect
25 cells using, for example, baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (*e.g.*, Sf 9 or Sf 21 cells) include the pAc series (Smith *et al.*, 1983) and the pVL series (Lucklow and Summers, 1989).

In yet another embodiment, a nucleic acid of the invention is expressed in
30 mammalian cells using a mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed, 1987) and pMT2PC (Kaufman *et al.*, 1987). When used in mammalian cells, the expression vector's control functions are often provided by viral regulatory elements.

As used herein, a promoter is a region of a DNA molecule typically within about 100 nucleotide pairs in front of (upstream of) the point at which transcription begins (*i.e.*, a transcription start site). That region typically contains several types of DNA sequence elements that are located in similar relative positions in different

5   genes. As used herein, the term "promoter" includes what is referred to in the art as an upstream promoter region, a promoter region or a promoter of a generalized eukaryotic RNA Polymerase II transcription unit.

Another type of discrete transcription regulatory sequence element is an enhancer. An enhancer provides specificity of time, location and expression level for

10   a particular encoding region (*e.g.*, gene). A major function of an enhancer is to increase the level of transcription of a coding sequence in a cell that contains one or more transcription factors that bind to that enhancer. Unlike a promoter, an enhancer can function when located at variable distances from transcription start sites so long as a promoter is present.

15   As used herein, the phrase "enhancer-promoter" means a composite unit that contains both enhancer and promoter elements. An enhancer-promoter is operatively linked to a coding sequence that encodes at least one gene product. As used herein, the phrase "operatively linked" means that an enhancer-promoter is connected to a coding sequence in such a way that the transcription of that coding

20   sequence is controlled and regulated by that enhancer-promoter. Means for operatively linking an enhancer-promoter to a coding sequence are well known in the art. As is also well known in the art, the precise orientation and location relative to a coding sequence whose transcription is controlled, is dependent *inter alia* upon the specific nature of the enhancer-promoter. Thus, a TATA box minimal promoter is

25   typically located from about 25 to about 30 base pairs upstream of a transcription initiation site and an upstream promoter element is typically located from about 100 to about 200 base pairs upstream of a transcription initiation site. In contrast, an enhancer can be located downstream from the initiation site and can be at a considerable distance from that site.

30   An enhancer-promoter used in a vector construct of the present invention can be any enhancer-promoter that drives expression in a cell to be transfected. By employing an enhancer-promoter with well-known properties, the level and pattern of gene product expression can be optimized.

For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus (CMV) and Simian Virus 40 (SV40). For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook *et al.*, "Molecular Cloning: A Laboratory Manual" 2nd, ed,

5   Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989, incorporated herein by reference.

In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (*e.g.*, tissue-specific regulatory elements are used to express the nucleic acid).

10   Tissue- specific regulatory elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert *et al.*, 1987), lymphoid-specific promoters (Calame and Eaton, 1988), in particular promoters of T cell receptors (Winoto and Baltimore, 1989) and immunoglobulins (Banerji *et al.*, 1983), Queen and Baltimore (1983), neuron-specific promoters (*e.g.*,

15   the neurofilament promoter; Byrne and Ruddle, 1989), pancreas-specific promoters (Edlund *et al.*, 1985), and mammary gland-specific promoters (*e.g.*, milk whey promoter; U.S. 4, 873,316 and EP 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss, 1990) and the α-fetoprotein promoter (Campes and Tilghman, 1989).

20   The invention further provides a recombinant expression vector comprising a DNA molecule encoding an *Alloiococcus otitidis* polypeptide cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operatively linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to

25   *Alloiococcus otitidis* mRNA. Regulatory sequences operatively linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The

30   antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced.

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but also to the

5   progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein. A host cell can be any prokaryotic or eukaryotic cell. For example, an *Alloiococcus otitidis* polypeptide can be expressed

10 in bacterial cells such as *Escherichia coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO), NIH3T3, PER C6, NSO, VERO or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA is can be introduced into prokaryotic or eukaryotic cells *via* conventional transformation, infection or transfection techniques. As used herein, the

15 terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (*e.g.*, DNA) into a host cell, including calcium phosphate or calcium chloride co-precipitation, DEAE-dextran-mediated transfection, lipofection, protoplast fusion, direct microinfection. Another recognized technique for introducing DNA into a host cell is "infection", such as by

20 adenovirus infection or electroporation. Suitable methods for transforming, infecting or transfecting host cells can be found in Sambrook, *et al.* ("Molecular Cloning: A Laboratory Manual" 2nd ed, Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989), and other laboratory manuals.

The most widely used method is transfection mediated by either calcium

25 phosphate or DEAE-dextran. Although the mechanism remains unclear, it is believed that the transfected DNA enters the cytoplasm of the cell by endocytosis and is transported to the nucleus. Depending on the cell type, up to 90% of a population of cultured cells can be transfected at any one time. Because of its high efficiency, transfection mediated by calcium phosphate or DEAE-dextran is the

30 method of choice for experiments that require transient expression of the foreign DNA in large numbers of cells. Calcium phosphate-mediated transfection is also used to establish cell lines that integrate copies of the foreign DNA, which are usually arranged in head-to-tail tandem arrays into the host cell genome.

In the protoplast fusion method, protoplasts derived from bacteria carrying high numbers of copies of plasmid of interest are mixed directly with cultured mammalian cells. After fusion of the cell membranes (usually with polyethylene glycol), the contents of the bacteria are delivered into the cytoplasm of the

5   mammalian cells and the plasmid DNA is transported to the nucleus. Protoplast fusion is not as efficient as transfection for many of the cell lines that are commonly used for transient expression assays, but it is useful for cell lines in which endocytosis of DNA occurs inefficiently. Protoplast fusion frequently yields multiple copies of the plasmid DNA tandemly integrated into the host chromosome.

10   The application of brief, high-voltage electric pulses (electroporation) to a variety of mammalian and plant cells leads to the formation of nanometer-sized pores in the plasma membrane. DNA is taken directly into the cell cytoplasm either through these pores or as a consequence of the redistribution of membrane components that accompanies closure of the pores. Electroporation can be extremely efficient and

15   can be used both for transient expression of cloned genes and for establishment of cell lines that carry integrated copies of the gene of interest. Electroporation, in contrast to calcium phosphate-mediated transfection and protoplast fusion, frequently gives rise to cell lines that carry one, or at most a few, integrated copies of the foreign DNA.

20   Liposome transfection involves encapsulation of DNA and RNA within liposomes, followed by fusion of the liposomes with the cell membrane. The mechanism of how DNA is delivered into the cell is unclear, but transfection efficiencies can be as high as 90%.

Direct microinjection of a DNA molecule into nuclei has the advantage of not

25   exposing DNA to cellular compartments such as low-pH endosomes. Microinjection therefore used primarily as a method to establish lines of cells that carry integrated copies of the DNA of interest.

The use of adenovirus as a vector for cell transfection is well known in the art. Adenovirus vector-mediated cell transfection has been reported for various cells

30   (Stratford-Perricaudet, et al. 1992).

A host cell of the invention, such as a prokaryotic or eukaryotic host cell in culture, is used to produce (i.e., express) an *Alloiococcus otitidis* polypeptide. Accordingly, the invention further provides methods for producing an *Alloiococcus*

otitidis polypeptide using the host cells of the invention. In one embodiment, the method comprises culturing the host cell of invention (into which a recombinant expression vector encoding an *Alloiococcus otitidis* polypeptide has been introduced) in a suitable medium until the *Alloiococcus otitidis* polypeptide is produced. In

5   another embodiment, the method further comprises isolating the *Alloiococcus otitidis* polypeptide from the medium or the host cell.

A coding sequence of an expression vector is operatively linked to a transcription-terminating region. RNA polymerase transcribes an encoding DNA sequence through a site where polyadenylation occurs. Typically, DNA sequences

10 located a few hundred base pairs downstream of the polyadenylation site serve to terminate transcription. Those DNA sequences are referred to herein as transcription-termination regions. Those regions are required for efficient polyadenylation of transcribed messenger RNA (mRNA). Transcription-terminating regions are well known in the art. A preferred transcription-terminating region used in

15 an adenovirus vector construct of the present invention comprises a polyadenylation signal of SV40 or the protamine gene.

An expression vector comprises a polynucleotide that encodes an *Alloiococcus otitidis* polypeptide. Such a polypeptide is meant to include a sequence of nucleotide bases encoding an *Alloiococcus otitidis* polypeptide sufficient in length

20 to distinguish the segment from a polynucleotide segment encoding a non-*Alloiococcus otitidis* polypeptide. A polypeptide of the invention can also encode biologically functional polypeptides or peptides which have variant amino acid sequences, such as with changes selected based on considerations such as the relative hydropathic score of the amino acids being exchanged. These variant

25 sequences are those isolated from natural sources or induced in the sequences disclosed herein using a mutagenic procedure such as site-directed mutagenesis.

Preferably, an expression vector of the present invention comprises a polynucleotide that encodes a polypeptide comprising the amino acid residue sequence of one of the even numbered sequences set forth in SEQ ID NO: 2 through

30 SEQ ID NO:.4036 An expression vector can include an *Alloiococcus otitidis* polypeptide coding region itself of any of the *Alloiococcus otitidis* polypeptides noted above or it can contain coding regions bearing selected alterations or modifications in the basic coding region of such an *Alloiococcus otitidis* polypeptide. Alternatively,

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such vectors or fragments can also encode larger polypeptides or polypeptides which nevertheless include the basic coding region. In any event, it should be appreciated that due to codon redundancy as well as biological functional equivalence, this aspect of the invention is not limited to the particular DNA molecules corresponding

5   to the polypeptide sequences noted above.

Exemplary vectors include the mammalian expression vectors of the pCMV family including pCMV6b and pCMV6c (Chiron Corp., Emeryville CA.). In certain cases, and specifically in the case of these individual mammalian expression vectors, the resulting constructs can require co-transfection with a vector containing a

10   selectable marker such as pSV2neo. *Via* co-transfection into a dihydrofolate reductase-deficient Chinese hamster ovary cell line, such as DG44, clones expressing *Alloiococcus otitidis* polypeptides by virtue of DNA incorporated into such expression vectors can be detected.

A DNA molecule of the present invention can be incorporated into a vector by

15   a number of techniques that are well known in the art. For instance, the vector pUC18 has been demonstrated to be of particular value in cloning and expression of genes. Likewise, the related vectors M13mp18 and M13mp19 can also be used in certain embodiments of the invention, in particular, in performing dideoxy sequencing.

20   An expression vector of the present invention is useful both as a means for preparing quantities of the *Alloiococcus otitidis* polypeptide-encoding DNA itself, and as a means for preparing the encoded polypeptide and peptides. It is contemplated that where *Alloiococcus otitidis* polypeptides of the invention are made by recombinant means, one can employ either prokaryotic or eukaryotic expression

25   vectors as shuttle systems. In another aspect, the recombinant host cells of the present invention are prokaryotic host cells. Preferably, the recombinant host cells of the invention are bacterial cells of the DH5α strain of *Escherichia coli*. In general, prokaryotes are preferred for the initial cloning of DNA sequences and constructing the vectors useful in the invention. For example, *Escherichia coli* K12 strains can be

30   particularly useful. Other microbial strains that can be used include *Escherichia coli* B, *Escherichia coli* W3110 (ATCC No. 273325) and *Escherichia. coli*$_x$1976 (ATCC No. 31537). *Bacilli* such as *Bacillus subtilis,* or other enterobacteriaceae such as *Salmonella typhimurium* or other *Salmonella* species or *Serratia marcesans,* and

various pseudomonas species can be used. These examples are, of course, intended to be illustrative rather than limiting.

In general, plasmid vectors containing replicon and control sequences that are derived from species compatible with the host cell are used in connection with these hosts. The vector ordinarily carries a replication site, as well as marking sequences that are capable of providing phenotypic selection in transformed cells. For example, Escherichia coli can be transformed using pBR322, a plasmid derived from an Escherichia coli species (Bolivar, et al. 1977). pBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells. The pBR322 plasmid, or other microbial plasmid or phage, must also contain, or be modified to contain, promoters which can be used by the microbial organism for expression of its own polypeptides.

Those promoters most commonly used in recombinant DNA construction include the β-lactamase (penicillinase) and lactose promoter systems (Chang, et al. 1978; Itakura., et al. 1977, Goeddel, et al. 1979; Goeddel, et al. 1980) and a tryptophan (TRP) promoter system (EP 0036776; Siebwenlist et al. 1980). While these are the most commonly used, other microbial promoters have been discovered and utilized, and details concerning their nucleotide sequences have been published, enabling a skilled worker to introduce functional promoters into plasmid vectors (Siebwenlist, et al. 1980).

In addition to prokaryotes, eukaryotic microbes such as yeast can also be used. Saccharomyces cerevisiase or common baker's yeast is the most commonly used among eukaryotic microorganisms, although a number of other strains are commonly available. For expression in Saccharomyces, the plasmid YRp7, for example, is commonly used (Stinchcomb, et al. 1979; Kingsman, et al. 1979; Tschemper, et al. 1980). This plasmid already contains the trpI gene that provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example ATCC No. 44076 or PEP4-1 (Jones, 1977). The presence of the trpI lesion as a characteristic of the yeast host cell genome then provides an effective environment for detecting transformation by growth in the absence of tryptophan.

Suitable promoter sequences in yeast vectors include the promoters for 3-phosphoglycerate kinase (PGK) (Hitzeman, et al. 1980) or other glycolytic enzymes (Hess, et al. 1968; Holland, et al. 1978) such as enolase, glyceraldehyde-3-

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phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase. In constructing suitable expression plasmids, the termination sequences

5   associated with these genes are also introduced into the expression vector downstream from the sequences to be expressed to provide polyadenylation of the mRNA and termination. Other promoters, which have the additional advantage of transcription controlled by growth conditions are the promoter region for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes

10   associated with nitrogen metabolism, and the aforementioned glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Any plasmid vector containing a yeast-compatible promoter, origin of replication, and termination sequences is suitable.

      In addition to microorganisms, cultures of cells derived from multicellular

15   organisms can also be used as hosts. In principle, any such cell culture is workable, whether from vertebrate or invertebrate culture. However, interest has been greatest in vertebrate cells, and propagation of vertebrate cells in culture (tissue culture) has become a routine procedure in recent years. Examples of such useful host cell lines are AtT-20, VERO, HeLa, NSO, PER C6, Chinese hamster ovary (CHO) cell lines,

20   W138, BHK, COSM6, COS-7, 293 , VERO and MDCK cell lines. Expression vectors for such cells ordinarily include (if necessary) an origin of replication, a promoter located upstream of the gene to be expressed, along with any necessary ribosome binding sites, RNA splice sites, polyadenylation site, and transcriptional terminator sequences.

25   Where expression of recombinant *Alloiococcus otitidis* polypeptides is desired and a eukaryotic host is contemplated, it is most desirable to employ a vector, such as a plasmid, that incorporates a eukaryotic origin of replication. Additionally, for the purposes of expression in eukaryotic systems, one desires to position the *Alloiococcus otitidis* encoding sequence adjacent to and under the control of an

30   effective eukaryotic promoter such as promoters used in combination with Chinese hamster ovary cells (CHO). To bring a coding sequence under control of a promoter, whether it is eukaryotic or prokaryotic, what is generally needed is to position the 5' end of the translation initiation side of the proper translational reading frame of the

polypeptide between about 1 and about 50 nucleotides 3' of or downstream with respect to the promoter chosen. Furthermore, where eukaryotic expression is anticipated, one would typically desire to incorporate an appropriate polyadenylation site into the transcriptional unit that includes the *Alloiococcus otitidis* polypeptide.

5   A transfected cell can be prokaryotic or eukaryotic. Preferably, the host cells of the invention are prokaryotic host cells. Where it is of interest to produce an *Alloiococcus otitidis* polypeptide, cultured prokaryotic host cells are of particular interest.

       In yet another embodiment, the present invention contemplates a process or
10   method of preparing *Alloiococcus otitidis* polypeptides comprising transfecting, transforming or infecting cells with a polynucleotide that encodes an *Alloiococcus otitidis* polypeptide to produce transformed host cells; and maintaining the transformed host cells under biological conditions sufficient for expression of the polypeptide. Preferably, the transformed host cells are prokaryotic cells.
15   Alternatively, the host cells are eukaryotic cells. More preferably, the prokaryotic cells are bacterial cells of the DH5α strain of *Escherichia coli*. Even more preferably, the polynucleotide transfected into the transformed cells comprises the nucleic acid sequence of one of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 105. Additionally, transfection is accomplished using an expression
20   vector disclosed above. A host cell used in the process is capable of expressing a functional, recombinant *Alloiococcus otitidis* polypeptide.

       Following transfection, the cell is maintained under culture conditions for a period of time sufficient for expression of an *Alloiococcus otitidis* polypeptide. Culture conditions are well known in the art and include ionic composition and concentration,
25   temperature, pH and the like. Typically, transfected cells are maintained under culture conditions in a culture medium. Suitable media for various cell types are well known in the art. In a preferred embodiment, temperature is from about 20°C to about 50°C, more preferably from about 30°C to about 40°C and, even more preferably about 37°C.
30   The pH is preferably from about a value of 6.0 to a value of about 8.0, more preferably from about a value of about 6.8 to a value of about 7.8 and, most preferably about 7.4. Osmolality is preferably from about 200 milliosmols per liter (mosm/L) to about 400 mosm/l and, more preferably from about 290 mosm/L to

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about 310 mosm/L. Other biological conditions needed for transfection and expression of an encoded protein are well known in the art.

Transfected cells are maintained for a period of time sufficient for expression of an *Alloiococcus otitidis* polypeptide. A suitable time depends *inter alia* upon the

5   cell type used and is readily determinable by a skilled artisan. Typically, maintenance time is from about 2 to about 14 days.

Recombinant *Alloiococcus otitidis* polypeptide is recovered or collected either from the transfected cells or the medium in which those cells are cultured. Recovery comprises isolating and purifying the *Alloiococcus otitidis* polypeptide. Isolation and

10   purification techniques for polypeptides are well known in the art and include such procedures as precipitation, filtration, chromatography, electrophoresis and the like.

F.   ANTIBODIES IMMUNOREACTIVE WITH *ALLOIOCOCCUS OTITIDIS* POLYPEPTIDES

15   In still another embodiment, the present invention provides antibodies immunoreactive with *Alloiococcus otitidis* polypeptides. Preferably, the antibodies of the invention are monoclonal antibodies. Additionally, the *Alloiococcus otitidis* polypeptides comprise the amino acid residue sequence of one of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106. Means

20   for preparing and characterizing antibodies are well known in the art (*See, e.g.*, Antibodies "A Laboratory Manual", E. Howell and D. Lane, Cold Spring Harbor Laboratory, 1988). Polyclonal antisera is obtained by bleeding an immunized animal into a glass or plastic container, incubating the blood at 25°C for one hour, followed by incubating at 4°C for 2-18 hours. The serum is then recovered by centrifugation.

25   Briefly, a polyclonal antibody is prepared by immunizing an animal with an immunogen comprising a polypeptide or polynucleotide of the present invention, and collecting antisera from that immunized animal. A wide range of animal species can be used for the production of antisera. Typically an animal used for production of anti-antisera is a rabbit, a mouse, a rat, a hamster or a guinea pig. Because of the

30   relatively large blood volume of rabbits, a rabbit is a preferred choice for production of polyclonal antibodies.

As is well known in the art, a given polypeptide or polynucleotide may vary in its immunogenicity. It is often necessary therefore to couple the immunogen (*e.g.*, a polypeptide or polynucleotide) of the present invention with a carrier. Exemplary and

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preferred carriers are keyhole limpet hemocyanin (KLH) and bovine serum albumin (BSA). Other albumins such as ovalbumin, mouse serum albumin or rabbit serum albumin can also be used as carriers.

5   Means for conjugating a polypeptide or a polynucleotide to a carrier protein are well known in the art and include glutaraldehyde, m-maleimidobencoyl-N-hydroxysuccinimide ester, carbodiimide and bis-biazotized benzidine.

As is also well known in the art, immunogencity to a particular immunogen can be enhanced by the use of non-specific stimulators of the immune response known as adjuvants. Exemplary and preferred adjuvants include complete Freund's

10   adjuvant, incomplete Freund's adjuvants, cholera toxin (e.g. mutant cholera toxin E29H; see published International Patent Application WO 00/18434), and aluminum hydroxide adjuvant.

The amount of immunogen used for the production of polyclonal antibodies depends upon the nature of the immunogen as well as the animal used for

15   immunization. A variety of routes can be used to administer the immunogen (subcutaneous, intramuscular, intradermal, intravenous and intraperitoneal). The production of polyclonal antibodies is monitored by sampling blood from the immunized animal at various points following immunization. When a desired level of immunogenicity is obtained, the immunized animal can be bled and the serum

20   isolated and stored.

In another aspect, the present invention contemplates a process of producing an antibody immunoreactive with an *Alloiococcus otitidis* polypeptide comprising the steps of (a) transfecting recombinant host cells with a polynucleotide that encodes an *Alloiococcus otitidis* polypeptide; (b) culturing the host cells under conditions

25   sufficient for expression of the polypeptide; (c) recovering the polypeptides; and (d) preparing the antibodies to the polypeptides. Preferably, the host cell is transfected with the polynucleotide of one of the odd numbered sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 4035. Even more preferably, the present invention provides antibodies prepared according to the process described above.

30   A monoclonal antibody of the present invention can be readily prepared through use of well-known techniques such as those exemplified in U.S. Pat. No. 4,196,265, herein incorporated by reference. Typically, a technique involves first immunizing a suitable animal with a selected antigen (*e.g.*, a polypeptide or

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polynucleotide of the present invention) in a manner sufficient to provide an immune response. Rodents such as mice and rats are preferred animals. Spleen cells from the immunized animal are then fused with cells of an immortal myeloma cell. Where the immunized animal is a mouse, a preferred myeloma cell is a murine NS-1

5   myeloma cell.

The fused spleen/myeloma cells are cultured in a selective medium to select fused spleen/myeloma cells from the parental cells. Fused cells are separated from the mixture of non-fused parental cells, e.g., by the addition of agents that block the de novo synthesis of nucleotides in the tissue culture media. Exemplary and

10   preferred agents are aminopterin, methotrexate, and azaserine. Aminopterin and methotrexate block de novo synthesis of both purines and pyrimidines, whereas azaserine blocks only purine synthesis. Where aminopterin or methotrexate is used, the media is supplemented with hypoxanthine and thymidine as a source of nucleotides. Where azaserine is used, the media is supplemented with

15   hypoxanthine.

This culturing provides a population of hybridomas from which specific hybridomas are selected. Typically, selection of hybridomas is performed by culturing the cells by single-clone dilution in microtiter plates, followed by testing the individual clonal supernatants for reactivity with an antigen-polypeptide. The

20   selected clones can then be propagated indefinitely to provide the monoclonal antibody.

By way of specific example, to produce an antibody of the present invention, mice are injected intraperitoneally with between about 1-200 μg of an antigen comprising a polypeptide of the present invention. B lymphocyte cells are stimulated

25   to grow by injecting the antigen in association with an adjuvant such as complete Freund's adjuvant (CFA; a non-specific stimulator of the immune response containing killed Mycobacterium tuberculosis). At some time (e.g., at least two weeks) after the first injection, mice are boosted by injection with a second dose of the antigen mixed with incomplete Freund's adjuvant (IFA; lacks the killed mycobacterium of CFA).

30   A few weeks after the second injection, mice are tail bled and the sera titered by immunoprecipitation against radiolabeled antigen. Preferably, the process of boosting and titering is repeated until a suitable titer is achieved. The spleen of the mouse with the highest titer is removed and the spleen lymphocytes are obtained by

homogenizing the spleen with a syringe. Typically, a spleen from an immunized mouse contains approximately $5x10^7$ to $2x10^8$ lymphocytes.

Mutant lymphocyte cells known as myeloma cells are obtained from laboratory animals in which such cells have been induced to grow by a variety of
5   well-known methods. Myeloma cells lack the salvage pathway of nucleotide biosynthesis. Because myeloma cells are tumor cells, they can be propagated indefinitely in tissue culture, and are thus denominated immortal. Numerous cultured cell lines of myeloma cells from mice and rats, such as murine NS-1 myeloma cells, have been established.

10   Myeloma cells are combined under conditions appropriate to foster fusion with the normal antibody-producing cells from the spleen of the mouse or rat injected with the antigen/polypeptide of the present invention. Fusion conditions include, for example, the presence of polyethylene glycol. The resulting fused cells are hybridoma cells. Like myeloma cells, hybridoma cells grow indefinitely in culture.

15   Hybridoma cells are separated from unfused myeloma cells by culturing in a selection medium such as HAT media (hypoxanthine, aminopterin, thymidine). Unfused myeloma cells lack the enzymes necessary to synthesize nucleotides from the salvage pathway because they are killed in the presence of aminopterin, methotrexate, or azaserine. Unfused lymphocytes also do not continue to grow in
20   tissue culture. Thus, only cells that have successfully fused (hybridoma cells) can grow in the selection media.

Each of the surviving hybridoma cells produces a single antibody. These cells are then screened for the production of the specific antibody immunoreactive with an antigen/polypeptide of the present invention. Single cell hybridomas are
25   isolated by limiting dilutions of the hybridomas. The hybridomas are serially diluted many times and, after the dilutions are allowed to grow, the supernatant is tested for the presence of the monoclonal antibody. The clones producing that antibody are then cultured in large amounts to produce an antibody of the present invention in convenient quantity.

30   By use of a monoclonal antibody of the present invention, specific · polypeptides and polynucleotide of the invention are identified as antigens. Once identified, those polypeptides and polynucleotide are isolated and purified by techniques such as antibody-affinity chromatography. In antibody-affinity

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chromatography, a monoclonal antibody is bound to a solid substrate and exposed to a solution containing the desired antigen. The antigen is removed from the solution through an immunospecific reaction with the bound antibody. The polypeptide or polynucleotide is then easily removed from the substrate and purified.

5   Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example, U.S. 5,223,409; WO 92/18619; WO 91/17271; WO 92/20791; WO 92/15679; WO 93/01288; WO 92/01047; WO 92/09690; WO 90/02809, which are incorporated herein in their entirety by reference.

10   Additionally, recombinant anti-*Alloiococcus otitidis* antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human fragments, which are made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies are produced by recombinant DNA techniques known in the art, for

15   example using methods described in PCT/US86/02269; EP 184,187; EP 171,496; EP 173,494; WO 86/01533; U.S. 4,816,567; and EP 125,023.

An anti-*Alloiococcus otitidis* antibody (*e.g.*, monoclonal antibody) is used to isolate *Alloiococcus otitidis* polypeptides by standard techniques, such as affinity chromatography or immunoprecipitation. An anti-*Alloiococcus otitidis* antibody

20   facilitates the purification of a natural *Alloiococcus otitidis* polypeptide from cells and · recombinantly produced *Alloiococcus otitidis* polypeptides expressed in host cells. Moreover, an anti-*Alloiococcus otitidis* antibody is used to detect *Alloiococcus otitidis* polypeptide (*e.g.*, in a cellular lysate or cell supernatant) in order to evaluate the abundance of the *Alloiococcus otitidis* polypeptide. The detection of circulating

25   fragments of an *Alloiococcus otitidis* polypeptide is used to identify *Alloiococcus otitidis* polypeptide turnover in a subject. Anti-*Alloiococcus otitidis* antibodies are used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, *e.g.*, to, for example, determine the efficacy of a given treatment regimen. Detection is facilitated by coupling (*i.e.*, physically linking) the antibody to a

30   detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, P-galactosidase, or

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acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a

5   luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and acquorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{15}S or ^{3}H.

G.   PHARMACEUTICAL COMPOSITIONS

10
In certain embodiments, the present invention provides pharmaceutical compositions comprising compounds that inhibit the activities of *Alloiococcus otitidis* polypeptides, and physiologically acceptable carriers. Compounds that inhibit the activities of *Alloiococcus otitidis* polypeptides polypeptides, which are essential for

15   the proliferation of the bacteria, are identified using one or more assay systems set forth in Examples 5-38. More preferably, the pharmaceutical compositions comprise one or more compounds that inhibit the activities of *Alloiococcus otitidis* polypeptides comprising the amino acid residue sequence of one or more of the even numbered sequences set forth in SEQ ID NO: 2 through SEQ ID NO: 106. In other

20   embodiments, the pharmaceutical compositions of the invention comprise antisense polynucleotides of polynucleotides selected from one of the odd numbered sequences set forth in Seq. ID NO. 1 to Seq. ID No. 105, and physiologically acceptable carriers.

Various tests are to be used to assess the *in vitro* and *in vivo* efficacy of

25   anitmicrobial and pharmaceutical compounds that inhibit the activities of *Alloiococcus otitidis* polypeptides, and these are set forth in detail in Examples 5 through 38. For example, an *in vitro* activity of the compounds may be assayed by incubating together a mixture of *Alloiococcus otitidis* or other heterologous bacterial cells such as *E. coli* cells expressing *Alloiococcus otitidis* polypeptides set forth in one of the

30   even numbered sequences from Seq. ID No. 2 to Seq. ID No. 106, and then measuring the activity of the polypeptide using one or more of the assay systems detailed in Example 5 through 38.

The *Alloiococcus otitidis* polynucleotides, polypeptides, compounds that modulate the activity of an *Alloiococcus otitidis* polypeptides, and anti-*Alloiococcus*

otitidis antibodies (also referred to herein as "active compounds") of the invention can be incorporated into pharmaceutical compositions suitable for administration to a host or subject, *e.g.*, a human. Such compositions typically comprise the nucleic acid molecule, protein, antimicrobial compound, or antibody and a pharmaceutically

5   acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active substances is well known in the art. Except

10   insofar as any conventional media or agent is incompatible with the active compound, such media can be used in the compositions of the invention. Supplementary active compounds can also be incorporated into the compositions.

A pharmaceutical of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include

15   parenteral, (*e.g.*, intravenous, intradermal, subcutaneous, intraperitoneal), transmucosal (*e.g.*, oral, rectal, intranasal, vaginal, respiratory), and transdermal (topical). Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol

20   or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or

25   sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water-soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersion. For

30   intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™(BASF, Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be fluid to the extent that easy syringability exists. It must be stable under the conditions of

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can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

For administration by inhalation, the compounds are delivered in the form of an aerosol spray from pressured container or dispenser that contains a suitable propellant, *e.g.*, a gas such as carbon dioxide, or a nebulizer. Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

The compounds can also be prepared in the form of suppositories (*e.g.*, with conventional suppository bases such as cocoa butter and other glycerides) or retention enemas for rectal delivery.

In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and microencapsulated delivery systems.

Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods

H.   DIAGNOSTIC ASSAYS

The invention also provides methods for detecting the presence of an *Alloiococcus otitidis* polypeptide or *Alloiococcus otitidis* polynucleotide, or fragment thereof, in a biological sample. The method involves contacting the biological sample

with a compound or an agent capable of detecting an *Alloiococcus otitidis*
polypeptide or mRNA such that the presence of the *Alloiococcus otitidis*
polypeptide/encoding nucleic acid molecule is detected in the biological sample. A
preferred agent for detecting *Alloiococcus otitidis* mRNA or DNA is a labeled or
5   labelable oligonucleotide probe capable of hybridizing to *Alloiococcus otitidis* mRNA
or DNA. The nucleic acid probe can be, for example, a full-length *Alloiococcus
otitidis* polynucleotide of one of the odd numbered sequences set forth in SEQ ID
NO: 1 through SEQ ID NO: 105, a complement thereof, or a fragment thereof, such
as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and
10   sufficient to specifically hybridize under stringent conditions to *Alloiococcus otitidis*
mRNA or DNA. Alternatively, the sample can be contacted with an oligonucleotide
primer of an *Alloiococcus otitidis* polynucleotide of SEQ ID NO: 1 through SEQ ID
:105, a complement thereof, or a fragment thereof, in the presence of nucleotides
and a polymerase, under conditions permitting primer extension.

15   A preferred agent for detecting *Alloiococcus otitidis* polypeptide is a labeled or
labelable antibody capable of binding to an *Alloiococcus otitidis* polypeptide.
Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or
a fragment thereof (*e.g.*, Fab or F(ab')2) can be used. The term "labeled or
labelable," with regard to the probe or antibody, is intended to encompass direct
20   labeling of the probe or antibody by coupling (*i.e.*, physically linking) a detectable
substance to the probe or antibody, as well as indirect labeling of the probe or
antibody by reactivity with another reagent that is directly labeled. Examples of
indirect labeling include detection of a primary antibody using a fluorescently labeled
secondary antibody and end-labeling of a DNA probe with biotin such that it can be
25   detected with fluorescently labeled streptavidin. The term "biological sample" is
intended to include tissues, cells and biological fluids isolated from a subject, as well
as tissues, cells and fluids present within a subject. That is, the detection method of
the invention can be used to detect *Alloiococcus otitidis* mRNA, DNA or protein in a
biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for
30   detection of *Alloiococcus otitidis* mRNA include Northern hybridizations and *in situ*
hybridizations. *In vitro* techniques for detection of *Alloiococcus otitidis* polypeptide
include enzyme linked immunosorbent assays (ELISAs), Western-blots,
immunoprecipitations and immunofluorescence. Alternatively, *Alloiococcus otitidis*

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polypeptides can be detected *in vivo* in a subject by introducing into the subject a labeled anti-*Alloiococcus otitidis* antibody. For example, the antibody can be labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

5   The polynucleotides according to the invention may also be used in analytical DNA chips, which allow sequencing, the study of mutations and of the expression of genes, and which are currently of interest given their very small size and their high capacity in terms of number of analyses.

The principle of the operation of these chips is based on molecular probes,
10   most often oligonucleotides, which are attached onto a miniaturized surface, generally of the order of a few square centimeters. During an analysis, a sample containing fragments of a target nucleic acid to be analyzed, for example DNA or RNA labeled, for example, after amplification, is deposited onto the DNA chip in which the support has been coated beforehand with probes. Bringing the labeled
15   target sequences into contact with the probes leads to the formation, through hybridization, of a duplex according to the rule of pairing defined by J.D. Watson and F. Crick. After a washing step, analysis of the surface of the chip allows the effective hybridizations to be located by means of the signals emitted by the labels tagging the target. A hybridization fingerprint results from this analysis which, by appropriate
20   computer processing, will make it possible to determine information such as the presence of specific fragments in the sample, the determination of sequences and the presence of mutations.

The chip consists of a multitude of molecular probes, precisely organized or arrayed on a solid support whose surface is miniaturized. It is at the center of a
25   system where other elements (imaging system, microcomputer) allow the acquisition and interpretation of a hybridization fingerprint.

The hybridization supports are provided in the form of flat or porous surfaces (pierced with wells) composed of various materials. The choice of a support is determined by its physicochemical properties, or more precisely, by the relationship
30   between the latter and the conditions under which the support will be placed during the synthesis or the attachment of the probes or during the use of the chip. It is therefore necessary, before considering the use of a particular support, to consider characteristics such as its stability to pH, its physical strength, its reactivity and its

chemical stability as well as its capacity to nonspecifically bind nucleic acids. Materials such as glass, silicon and polymers are commonly used. Their surface is, in a first step, called "functionalization", made reactive towards the groups which it is desired to attach thereon. After the functionalization, so-called spacer molecules are

5   grafted onto the activated surface. Used as intermediates between the surface and the probe, these molecules of variable size render unimportant the surface properties of the supports, which often prove to be problematic for the synthesis or the attachment of the probes and for the hybridization.

         Among the hybridization supports, there may be mentioned glass which is

10   used, for example, in the method of *in situ* synthesis of oligonucleotides by photochemical addressing developed by the company Affymetrix (E.L. Sheldon, 1993), the glass surface being activated by silane. Genosensor Consortium (P. Mérel, 1994) also uses glass slides carrying wells 3 mm apart, this support being activated with epoxysilane.

15   The probes according to the invention may be synthesized directly *in situ* on the supports of the DNA chips. This *in situ* synthesis may be carried out by photochemical addressing (developed by the company Affymax (Amsterdam, Holland) and exploited industrially by its subsidiary Affymetrix (United States)) or based on the VLSIPS (very large scale immobilized polymer synthesis) technology

20   (S.P.A. Fodor *et al.*, 1991) which is based on a method of photochemically directed combinatory synthesis and the principle of which combines solid-phase chemistry, the use of photolabile protecting groups and photolithography.

         The probes according to the invention may be attached to the DNA chips in various ways such as electrochemical addressing, automated addressing or the use

25   of probe printers (T. Livache *et al.*, 1994; G. Yershov *et al.*, 1996; J. Derisi *et al.*, 1996, and S. Borman, 1996).

         The revealing of the hybridization between the probes of the invention, deposited or synthesized *in situ* on the supports of the DNA chips, and the sample to be analyzed, may be determined, for example, by measurement of fluorescent

30   signals, by radioactive counting or by electronic detection.

         The use of fluorescent molecules such as fluorescein constitutes the most common method of labeling the samples. It allows direct or indirect revealing of the hybridization and allows the use of various fluorochromes.

Affymetrix currently provides an apparatus or a scanner designed to read its Gene Chip™ chips. It makes it possible to detect the hybridizations by scanning the surface of the chip in confocal microscopy (R.J. Lipshutz *et al.*, 1995).

The nucleotide sequences according to the invention are also used in DNA

5   chips to carry out the analysis of the expression of the *Alloiococcus otitidis* genes. This analysis of the expression of *Alloiococcus otitidis* genes is based on the use of chips where probes of the invention, chosen for their specificity to characterize a given gene, are present (D.J. Lockhart *et al.*, 1996; D.D. Shoemaker *et al.*, 1996). For the methods of analysis of gene expression using the DNA chips, reference may,

10   for example, be made to the methods described by D.J. Lockhart *et al.* (1996) and Sosnowsky *et al.* (1997) for the synthesis of probes *in situ* or for the addressing and the attachment of previously synthesized probes. The target sequences to be analyzed are labeled and in general fragmented into sequences of about 50 to 100 nucleotides before being hybridized onto the chip. After washing as described,

15   for example, by D.J. Lockhart *et al.* (1996) and application of different electric fields (Sosnowsky *et al.*, 1997), the labeled compounds are detected and quantified, the hybridizations being carried out at least in duplicate. Comparative analyses of the signal intensities obtained with respect to the same probe for different samples and/or for different probes with the same sample, determine the differential

20   expression of RNA or of DNA derived from the sample.

The nucleotide sequences according to the invention are, in addition, used in DNA chips where other nucleotide probes specific for other microorganisms are also present, and allow the carrying out of a serial test allowing rapid identification of the presence of a microorganism in a sample:

25   Accordingly, the subject of the invention is also the nucleotide sequences according to the invention, characterized in that they are immobilized on a support of a DNA chip.

The DNA chips, characterized in that they contain at least one nucleotide sequence according to the invention, immobilized on the support of the said chip,

30   also form part of the invention.

The chips preferably contain several probes or nucleotide sequences of the invention of different length and/or corresponding to different genes so as to identify, with greater certainty, the specificity of the target sequences or the desired mutation

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in the sample to be analyzed.

Accordingly, the analyses carried out by means of primers and/or probes according to the invention, immobilized on supports such as DNA chips, make it possible, for example, to identify, in samples, mutations linked to variations such as intraspecies variations. These variations may be correlated or associated with pathologies specific to the variant identified and make it possible to select the appropriate treatment.

The invention thus comprises a DNA chip according to the invention, characterized in that it contains, in addition, at least one nucleotide sequence of a microorganism different from *Alloiococcus otitidis,* immobilized on the support of the said chip; preferably, the different microorganism is chosen from an associated microorganism, a bacterium of the *Streptococcus* family, and a variant of the species *Alloiococcus otitidis.*

The principle of the DNA chip as explained above, is also used to produce protein "chips" on which the support has been coated with a polypeptide or an antibody according to the invention, or arrays thereof, in place of the DNA. These protein "chips" make it possible, for example, to analyze the biomolecular interactions (BIA) induced by the affinity capture of target analytes onto a support coated, for example, with proteins, by surface plasma resonance (SPR). Reference may be made, for example, to the techniques for coupling proteins onto a solid support which are described in EP 524 800 or to the methods describing the use of biosensor-type protein chips such as the BIAcore-type technique (Pharmacia) (Arlinghaus *et al.,* 1997, Krone *et al.,* 1997, Chatelier *et al.,* 1995). These polypeptides or antibodies according to the invention, capable of specifically binding antibodies or polypeptides derived from the sample to be analyzed, are thus used in protein chips for the detection and/or the identification of proteins in samples. The said protein chips may in particular be used for infectious diagnosis and preferably contain, per chip, several polypeptides and/or antibodies of the invention of different specificity, and/or polypeptides and/or antibodies capable of recognizing microorganisms different from *Alloiococcus otitidis.*

Accordingly, the subject of the present invention is also the polypeptides and the antibodies according to the invention, characterized in that they are immobilized on a support, in particular, on a protein chip.

The protein chips, characterized in that they contain at least one polypeptide or one antibody according to the invention immobilized on the support of the said chip, also form part of the invention.

The invention comprises, in addition, a protein chip according to the invention,

5 characterized in that it contains, in addition, at least one polypeptide of a microorganism different from *Alloiococcus otitidis* or at least one antibody directed against a compound of a microorganism different from *Alloiococcus otitidis*, immobilized on the support of the chip.

The invention also relates to a kit or set for the detection and/or the

10 identification of bacteria belonging to the species *Alloiococcus otitidis* or to an associated microorganism, or for the detection and/or the identification of a microorganism characterized in that it comprises a protein chip according to the invention.

The present invention also provides a method for the detection and/or the

15 identification of bacteria belonging to the species *Alloiococcus otitidis* or to an associated microorganism in a biological sample, characterized in that it uses a nucleotide sequence according to the invention.

The invention also encompasses kits for detecting the presence of an *Alloiococcus otitidis* polypeptide in a biological sample. For example, the kit

20 comprises reagents such as a labeled or labelable compound or agent capable of detecting *Alloiococcus otitidis* polypeptide or mRNA in a biological sample; means for determining the amount of *Alloiococcus otitidis* polypeptide in the sample; and means for comparing the amount of *Alloiococcus otitidis* polypeptide in the sample with a standard. The compound or agent are packaged in a suitable container. The kit

25 further comprises instructions for using the kit to detect *Alloiococcus otitidis* mRNA or protein.

In certain embodiments, detection involves the use of a probe/primer in a polymerase chain reaction (PCR) (*see, e.g.* U.S. 4,683,195 and U.S. 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction

30 (LCR). This method includes the steps of collecting a sample of cells from a patient, isolating nucleic acid (*e.g.*, genomic, mRNA or both) from the cells of the sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to an *Alloiococcus otitidis* polynucleotide under conditions such that

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hybridization and amplification of the *Alloiococcus otitidis*-polynucleotide (if present) occurs, and detecting the presence or absence of an amplification product, or detecting the size of the amplification product and comparing the length to a control sample.

5

I.　TRANSGENIC ANIMALS

It is contemplated that in some instances the genome of a transgenic animal of the present invention will have been altered through the stable introduction of one
10　or more of the *Alloiococcus otitidis* polynucleotide compositions described herein, either native, synthetically modified or mutated. As described herein, a "transgenic animal" refers to any animal, preferably a non-human mammal (*e.g.* mouse, rat, rabbit, squirrel, hamster, rabbits, guinea pigs, pigs, micro-pigs, baboons, squirrel monkeys and chimpanzees, *etc*), bird or an amphibian, in which one or more cells
15　contain a heterologous nucleic acid sequence introduced by way of human intervention, such as by transgenic techniques well known in the art. The nucleic acid is introduced into the cell, directly or indirectly, by introduction into a precursor of the cell, by way of deliberate genetic manipulation, such as by microinjection or by infection with a recombinant virus. The term genetic manipulation does not include
20　classical crossbreeding, or *in vitro* fertilization, but rather is directed to the introduction of a recombinant DNA molecule. This molecule may be integrated within a chromosome, or it may be extrachromosomally replicating DNA.

The host cells of the invention are also used to produce non-human transgenic animals. The non-human transgenic animals are used in screening
25　assays designed to identify infections or compounds, *e.g.,* drugs, pharmaceuticals, *etc.,* which are capable of ameliorating *Alloiococcus otitidis* symptoms or infections. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which an *Alloiococcus otitidis* polypeptide-coding sequence has been introduced. Such host cells are then used to create non-human
30　transgenic animals in which exogenous *Alloiococcus otitidis* gene sequences have been introduced into their genome or homologous recombinant animals in which endogenous *Alloiococcus otitidis* gene sequences have been altered. Such animals are useful for studying the effects of an *Alloiococcus otitidis* polypeptide and for

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identifying and/or evaluating modulators of *Alloiococcus otitidis* polypeptide infectivity.

A transgenic animal of the invention is created by introducing an *Alloiococcus otitidis* polypeptide-encoding nucleic acid sequence into the male pronuclei of a fertilized oocyte, *e.g.*, by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The human *Alloiococcus otitidis* cDNA sequence of one or more of SEQ ID NO:1 through SEQ ID NO: 4035 can be introduced as a transgene into the genome of a non-human animal.

Moreover, a non-*Alloiococcus otitidis* homologue of the *Alloiococcus otitidis* gene can be isolated based on hybridization to the *Alloiococcus otitidis* cDNA (described above) and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the *Alloiococcus otitidis* transgene to direct expression of an *Alloiococcus otitidis* polypeptide to particular cells. Methods for generating transgenic animals *via* embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. 4,736,866 and 4,870, 009, U.S. 4,873,191 and in Hogan, 1986. Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the *Alloiococcus otitidis* transgene in its genome and/or expression of *Alloiococcus otitidis* mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding an *Alloiococcus otitidis* polypeptide can further be bred to other transgenic animals carrying other transgenes.

In another embodiment, transgenic non-human animals can be produced which contain selected systems that allow for regulated expression of the transgene. One example of such a system is the cre/loxP recombinase system of bacteriophage PλI. For a description of the cre/loxP recombinase system, *see, e.g.*, Lakso *et al.*, 1992. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gon-nan *et al.*, 1991). If a cre/loxP recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required.

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Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

5   Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al., 1997, and PCT International Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G_o phase. The quiescent cell can then be fused, e.g., through

10   the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyst and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is

15   isolated.

All patents and publications cited herein are hereby incorporated by reference.

The following examples are carried out using standard techniques, which are well known and routine to those of skill in the art, except where otherwise described

20   in detail. The following examples are presented for illustrative purposes, and should not be construed in any way limiting the scope of this invention.

EXAMPLE 1

CONFIRMATION OF THE IDENTITY OF THE *ALLOIOCOCCUS OTITIDIS* 1104-92 ISOLATE

25

The *Alloiococcus otitidis* isolate 1104-92 was obtained from Dr. Richard Facklam of the Centers for Disease Control in Atlanta. It was isolated from the middle ear fluid of a child in the Atlanta, Georgia area. It was confirmed to be *A. otitidis* by comparing it to the type strain, ATCC51267, obtained from the American Type

30   Culture Collection [Aguirre, 1992 #1]. Both the 1104-92 and type strain are characterized as Gram positive cocci. Both grow on Columbia agar supplemented with 5% yeast extract, 0.5% polysorbate 80 (Tween 80), and 0.7% phospatidyl choline when incubated at 37°C. On this medium, both strains form slow growing

small white colonies that require nearly two days to be easily observed with the naked eye. Both are sensitive to lysis by hen egg white lysozyme and *Streptococcus globisporus* mutanolysin. Both grow in the presence of 2% sodium azide. Both are killed by incubation at 55°C for 30 minutes. Finally, to further confirm that the 1104-92 was a strain of *A. otitidis*, it was subject to polymerase chain reaction (PCR) identification based on its 16s rRNA gene. This was done using two of the primers specified by Aguirre and Collins [Aguirre, 1992 #2]. The antisense primer used was

5'-ATCTTCCTGCTTGCAGGAAGAGG-3' and the sense primer was

3'-CGCTTCATCTCTGAAGCTAGC-5'. Thus by multiple criteria, the 1104-92 strain was confirmed to be an isolate of *A. otitidis*.

EXAMPLE 2

STORAGE, GROWTH, AND HARVEST OF *ALLOIOCOCCUS OTITIDIS* 1104-92 FOR ISOLATION OF DNA

The *A. otitidis* isolate 1104-92 was stored at –70°C in Todd-Hewlett broth containing 40% glycerol. A small portion of the frozen stock was streaked onto the agar medium described in Example 1 and incubated at 37°C for two days. The growth from the plate was swabbed into a 17 x 100 cm tube containing 6 ml of a serum-free broth medium. This broth medium was prepared with 30 g Todd-Hewlett medium, 5 g yeast extract, 10 ml polysorbate 80 (Tween 80), and 1 liter distilled water. This medium was sterilized by autoclaving for 35 minutes. The bacteria were incubated aerobically without shaking in an aerobic incubator at 37°C for two days. The tube containing the growing bacteria was then shaken to resuspend the bacteria and added to a liter of the same medium in a Fernbach flask. This flask, in turn, was incubated aerobically for three days without shaking. The bacteria were harvested by first swirling the flask to suspend the bacteria and then low speed centrifugation at about 5,000 x g for 30 minutes. The pellet of bacteria was washed by resuspending it in 10 to 15 mL of phosphate buffered saline (PBS), and centrifuging the suspension at about 8,000 x g for 20 minutes. The pellet of bacteria was retained and stored frozen at -20°C. The yield of wet bacterial pellet was typically about 1 g per liter of broth.

EXAMPLE 3

PREPARATION OF *ALLOIOCOCCUS OTITIDIS* GENOMIC DNA

To prepare genomic DNA, 0.95 g frozen pellet of bacteria was defrosted and
5   suspended in 10 mL of PBS containing 1 mM $MgCl_2$. The bacteria were killed by
incubating the suspension at 55°C for 20 minutes. The suspension was allowed to
cool before adding 25 μl of a 10 mg/mL stock of hen egg white lysozyme and 50 μl of
a 25,000 unit/mL stock of *Streptococcus globisporus* mutanolysin to the suspension.
It was then incubated for one hour at 37°C. Then 50 μl of a 10 mg/mL stock of
10   RNase was added and the suspension incubated an additional hour at 37°C. After
these incubations, sodium dodecylsulfate (SDS) was added to a final concentration
of 0.3% (0.3 mL of a 10% stock). This was followed by the addition of 0.3 mL of a 1
mg/mL stock of proteinase K. The suspension was then incubated for two hours at
37°C. After this time, an equal volume of water saturated phenol/chloroform/isopropyl
15   (25:24:1) was added to the digested suspension and gently mixed. The upper
aqueous layer was retained after a low speed centrifugation and 2.5 volumes of
ethanol were added and the tube gently inverted to mix. The DNA was then spooled
out on a glass rod and allowed to air dry.

The DNA at this stage still contained obvious impurities and needed further
20   purification. The DNA dried on the glass rod was soaked in 70% ethanol to remove
excess phenol and air-dried once again. It was then suspended in 2 ml of Tris-EDTA
buffer to which 2 μl of RNase cocktail was added and incubated at room temperature
for 75 minutes. Then 100 μl of protease, 100 μl SDS and 40 μl of 100 mM $CaCl_2$
were added and the suspension incubated for 3.5 hours. An equal volume of
25   chloroform was added, gently mixed, then centrifuged at a low speed. The aqueous
layer was collected and re-extracted with the phenol, chloroform, isopropyl alcohol
reagent. In turn, the aqueous layer was extracted with chloroform. At this point, 3 M
sodium acetate was added to the aqueous phase collected form the last extraction
and then 3.75 ml of ethanol was added and gently mixed. The DNA was spooled out,
30   soaked in 70% ethanol and allowed to air-dry. The DNA was finally suspended in 2
ml of Tris-EDTA buffer. Based on absorption at 260 nm, the final yield of DNA was
482 μg of DNA. The DNA was confirmed to be that of *A. otitidis* by the PCR method
described in example 1. This DNA was submitted for sequencing.

EXAMPLE 4

CLONING AND SEQUENCING *ALLOIOCOCCUS OTITIDIS* GENOME

5   This invention provides nucleotide sequences of the genome of *Alloiococcus otitidis*
which thus comprises a DNA sequence library of *Alloiococcus otitidis* genomic DNA.
The detailed description that follows provides nucleotide sequences of Alloiococcus
otitidis, and also describes how the sequences were obtained and how ORFs (Open
Reading Frames) and protein-coding sequences can be identified.

10   To construct a library, genomic DNA was hydrodynamically sheared in an
HPLC and then separated on a standard 1% agarose gel. A fraction corresponding
to 3000-3500 bp in length was excised from the gel and purified by the GeneClean
procedure (BIO101, Inc.).

       The purified DNA fragments were then blunt-ended using T4 DNA

15   polymerase. The blunt-ended DNA was then ligated to unique BstX1-linker adapters.
These linkers are complimentary to the pGTC vector, while the overhang is not self-
complimentary. Therefore, the linkers will not concatermerize nor will the cut-vector
religate itself easily. The liner-adapted inserts were separated from the
unincorporated linkers on a 1% agarose gel and again purified using GeneClean.

20   The linker-adapted inserts were then ligated to BstX1-cut vector to construct
"shotgun" subclone libraries.

       Only major modifications to the protocols are highlighted. Briefly, the library
was transformed into DH10B competent cells (Gibco/BRL, DH5a transformation
protocol). Transformed cells were detected by plating onto antibiotic plates

25   containing ampicillin. The plates were incubated overnight at 37° C. Transformant
clones were then selected for sequencing. The cultures were grown overnight at
37°C. DNA was purified using a silica bead DNA preparation (Egelstein, 1996)
method. In this manner, 25 mg of DNA was obtained per clone.

       These purified DNA samples were then sequenced using ABI dye-terminator

30   chemistry. All subsequent steps were based on sequencing by automated DNA
sequencing methods. The ABI dye terminator sequence reads were run on
MegaBace™ 10000 (Amersham) machines and the data transferred to UNIX based
computers. Base calls and quality scores were determined using the PHRED

software program (Ewing et al., 1998, Genome Res. 8: 175-185; Ewing and Green, 1998, Genome Res. 8:685-734). Reads were assembled using PHRAP (P. Green, Abstracts of DOE Human Genome Program Contractor-Grantee Workshop V, Jan. 1996, p 157) with default program parameters and quality scores.

5   To identify *Alloiococcus otitidis* genome encoded polypeptides, the complete genomic sequence of *Alloiococcus otitidis* was analyzed essentially as follows: First, all possible stop-to-stop open reading frames (ORFs) ≥ 222 nucleotides in all three reading frames were translated into amino acid sequences.

Second, the identified ORFs were analyzed for homology to known protein 10 sequences. Third, the coding potential of non-homologous sequences were evaluated with the GENEMARKTM software program (Borodovsky and McIninch, 1993, Comp. Chem. 17:123). The results of these analysis are set forth in tables 2-16.

15   EXAMPLE 5

IDENTIFICATION OF SPECIFIC GENES IN ALLOIOCOCCUS OTITIDIS

Alloiococcus otitidis homologs of the genes listed in Table 4 were identified as follows:

20   Protein sequences of interest ("query sequences", Table 4) were extracted from Genbank from one or more species; query species included but were not limited to *Staphylococcus aureus, Streptococcus pnuemoniae, Streptococcus pyogenes, Lactococcus lactis, Escherichia coli,* and *Bacillus subtilis.* These queries were compared to the *Alloiococcus otitidis* sequence by several methods in order to 25 determine which *Alloiococcus* sequence was the ortholog for the query gene.

First, the query sequences were compared to the translated *Alloiococcus otitidis* ORF set using BLASTP. The ORF set was generated as described in Vaccines patent, except that for each ORF that had multiple potential start codons, only the longest ORF was used. The top 10 *Alloiococcus otitidis* hits for each query 30 were saved, without regard to score.

These *Alloiococcus otitidis* hits were then compared to NR, the nonredundant Genpept database, using BLASTP. An *Alloiococcus otitidis* ORF was considered the ortholog of a query sequence if the genes were reciprocal best hits in *Alloiococcus*

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otitidis and the query genome.   This analysis is also sumarized in Table 4 (excel file AOT_PATENT_FILE.xls, Sheet TopHitsAndClustalKey). Specific numerical cutoffs were not used; however all top hits had Expect values of less than 3×10^{-28}.

Several query sequences had more than one high-scoring hit in *Alloiococcus*

5   *otitidis*. In most cases, however, only the first, best hit to the original query sequence had that query sequence as its reciprocal best hit. For example, the *Streptococcus pyogenes* query sequence GyrA (alpha subunit of DNA gyrase) has two high-scoring hits in *Alloiococcus otitidis*. These were distinguished by the reciprocal blast analysis; the first, ORF_505 (60% identity, Expect = 0) is the GyrA homolog and the

10   second, ORF_1907 (38% identity, Expect = 1×10^{-154}) is the homolog of the query sequence GrlA or ParC (topoisomerase IV, A subunit).   Other examples of closely related proteins include the B subunits of DNA gyrase (GyrB) and Topoisomerase IV (GrlB or ParE); and YphC and Era, both of which are putative GTP binding proteins of unknown function. These *Alloiococcus otitidis* ORFS were assigned based on

15   their top hit in Genpept.

In two cases the multiple high-scoring hits in *Alloiococcus otitidis* were the result of gene duplication. In the case of MurA (UDP-N-acetylglucosamine enolpyruvyl transferase) two separate *Alloiococcus otitidis* ORFS were determined to be the desired orthologs, because both had MurA (or MurZ, alternate notation) as

20   their best hit in Genpept. Likewise, there are two FolC (folylpolyglutamate synthase) homologs in *Alloiococcus otitidis*. It is known that other bacteria, particularly Gram-positive bacteria, may carry two homologs of each of these genes.

As a further step in verification of gene assignments, the *Alloiococcus otitidis* ORFS identified as orthologs of the query genes by the analysis above were then

25   compared to an internal copy of the COGS database (Tatusov RL, Natale DA, Garkavtsev IV, Tatusova TA, Shankavaram UT, Rao BS, Kiryutin B, Galperin MY, Fedorova ND, Koonin EV, 2001, Nucleic Acids Res 2001 Jan 1;29(1):22-8. The COG database: new developments in phylogenetic classification of proteins from complete genomes) using BLASTP. The COGS database is a curated set of proteins

30   from a set of finished bacterial genomes, which have been grouped into specific protein families on the basis of protein similarity.   In all cases, the *Alloiococcus otitidis* ORF was most closely related to the COGS family of the initial query protein, if that protein had been assigned to a COGS family. Examples of proteins for which

there is no COGS family defined (in our local version of the database) include SrtA (sortase) and MvaK1 (phosphomevalonate kinase).

As a final confirmation, all query proteins were compared to the complete *Alloiococcus otitidis* nucleotide sequence using TBLASTN, in order to determine if there were additional and/or better hits that had not been predicted as ORFS. In all cases, the same sequence was identified as the best hit by TBLASTN and by BLASTP.

For one query sequence, sortase, the *Alloiococcus otitidis* ORF that was the top hit (Expect = 0.42) by the initial BLASTP or TBLASTN using the *Staphylococcus aureus* sortase sequence as query was found by additional analysis (reciprocal blast) to be a putative ABC-transport protein. The true sortase homolog in *Alloiococcus otitidis* was identified by construction of a Hidden Markov Model based on a multiple alignment of 72 known and putative sortase proteins that had been identified previously using similar computational methods. The model was constructed using "hmmbuild" and the *Alloiococcus otitidis* ORF set was searched using "hmmsearch", both of the hmmer package (S.R. Eddy. Profile hidden Markov models. *Bioinformatics* 14:755-763, 1998). The assignment of ORF_876 as sortase was then confirmed by reciprocal blast as described above and in Table 2. ORF_876 was also found to be the top hit in *Alloiococcus otitidis* when the *Bacillus subtilis* putative sortase (YhcS) was used as the query sequence in a BLASTP search. The *Bacillus halodurans* BH3596 *Bacillus subtilis* YhcS and proteins that are the top hits for RF_876 have recently been placed into a COGS group of sortases, further confirming the identity of ORF_876 as the *Alloiococcus otitidis* sortase.

TABLE 4

ORF NO.	DNA SEQ ID NO.r	ORF Start	Protein Start	ORF Stop	Protein SEQ ID No.	Gene
46b	Seq. ID No. 1	26225	26153	25800	Seq. ID No. 2	ACPS
48c	Seq. ID No. 3	29105	29090	27696	Seq. ID No. 4	murF
57b	Seq. ID No. 5	33738	33732	32455	Seq. ID No. 6	murA-2
65c	Seq. ID No. 7	37245	37242	36634	Seq. ID No. 8	rpoE
172	Seq. ID No. 9	88726	88726	87785	Seq. ID No. 10	rpoA
228d	Seq. ID No. 11	111563	111542	107883	Seq. ID No. 12	rpoC
236c	Seq. ID No. 13	115224	115221	111643	Seq. ID No. 14	rpoB
495c	Seq. ID No. 15	247355	247331	245949	Seq. ID No. 16	dnaB/C
505b	Seq. ID No. 17	254277	254268	251794	Seq. ID No. 18	gyrA
509	Seq. ID No. 19	256252	256246	254297	Seq. ID No. 20	gyrB
515c	Seq. ID No. 21	259131	259116	257914	Seq. ID No. 22	dnaN
528b	Seq. ID No. 23	263837	263861	265153	Seq. ID No. 24	folC-2
851b	Seq. ID No. 25	440982	441072	442634	Seq. ID No. 26	murE
876	Seq. ID No. 27	453874	453898	454509	Seq. ID No. 28	srtA
956	Seq. ID No. 29	500019	500019	501308	Seq. ID No. 30	folC-1
959	Seq. ID No. 31	501978	501993	502364	Seq. ID No. 32	folB
961c	Seq. ID No. 33	502392	502413	502943	Seq. ID No. 34	folK
1183b	Seq. ID No. 35	626391	626430	627632	Seq. ID No. 36	mvaS
1184	Seq. ID No. 37	629315	629285	627993	Seq. ID No. 38	mvaA
1263	Seq. ID No. 39	675596	675608	676525	Seq. ID No. 40	murB
1273	Seq. ID No. 41	685392	685377	684289	Seq. ID No. 42	mvaK2
1275b	Seq. ID No. 43	686415	686403	685393	Seq. ID No. 44	mvaD
1277	Seq. ID No. 45	687376	687349	686396	Seq. ID No. 46	mvaK1
1279	Seq. ID No. 47	687461	687506	688435	Seq. ID No. 48	coaA
1284	Seq. ID No. 49	691675	691681	692520	Seq. ID No. 50	nadE
1511	Seq. ID No. 51	815078	815084	815920	Seq. ID No. 52	murI
1811b	Seq. ID No. 53	985498	985504	986454	Seq. ID No. 54	folP
1863b	Seq. ID No. 55	1019023	1019050	1019583	Seq. ID No. 56	folA
1902	Seq. ID No. 57	1040639	1040645	1042606	Seq. ID No. 58	GrlB
1907	Seq. ID No. 59	1042729	1042732	1045191	Seq. ID No. 60	grlA

Table 4
(Cont'd.)

ORF NO.	DNA SEQ ID NO.r	ORF Start	Protein Start	ORF Stop	Protein SEQ ID No.	Gene
1990c	Seq. ID No. 61	1098801	1098798	1097689	Seq. ID No. 62	rpoD
1992b	Seq. ID No. 63	1100670	1100670	1098817	Seq. ID No. 64	dnaG
2003	Seq. ID No. 65	1109198	1109144	1108212	Seq. ID No. 66	era
2016h	Seq. ID No. 67	1115435	1115390	1113879	Seq. ID No. 68	norA
2133	Seq. ID No. 69	1179995	1179938	1175604	Seq. ID No. 70	polC
2181b	Seq. ID No. 71	1203606	1203588	1202281	Seq. ID No. 72	obg
2204	Seq. ID No. 73	1216828	1216804	1215491	Seq. ID No. 74	yphC
2240c	Seq. ID No. 75	1236616	1236607	1233293	Seq. ID No. 76	dnaE
2284	Seq. ID No. 77	1261069	1261063	1259858	Seq. ID No. 78	coaBC
2328	Seq. ID No. 79	1286689	1286668	1285637	Seq. ID No. 80	holA
2333	Seq. ID No. 81	1290847	1290847	1290371	Seq. ID No. 82	coaD
2485	Seq. ID No. 83	1374427	1374400	1373168	Seq. ID No. 84	ftsZ
2489	Seq. ID No. 85	1375804	1375792	1374428	Seq. ID No. 86	ftsA
2492b	Seq. ID No. 87	1378075	1378060	1376897	Seq. ID No. 88	murG
2494	Seq. ID No. 89	1379477	1379453	1378050	Seq. ID No. 90	murD
2514	Seq. ID No. 91	1390141	1390135	1389491	Seq. ID No. 92	nadD
2596	Seq. ID No. 93	1437374	1437374	1436709	Seq. ID No. 94	coaE
2602	Seq. ID No. 95	1442399	1442396	1441065	Seq. ID No. 96	murC
2645	Seq. ID No. 97	1467800	1467782	1466751	Seq. ID No. 9	fmhB
2875	Seq. ID No. 99	1605944	1605923	1603701	Seq. ID No. 100	pcrA
2918	Seq. ID No. 101	1631092	1631089	1629779	Seq. ID No. 102	murA-1
3001	Seq. ID No. 103	1680254	1680221	1679229	Seq. ID No. 104	holB
3012	Seq. ID No. 105	1684114	1684102	1682330	Seq. ID No. 106	dnaX

EXAMPLE 6

IDENTIFICATION OF THE GENE ENCODING COENZYME A (COA) IN *ALLOIOCOCCUS OTITIDIS*

Pantothenate kinase (PanK, CoaA) encoded by the *coaA* gene catalyzes the initial step in Coenzyme A (CoA) biosynthesis. CoA is an essential co-factor in a number of metabolic pathways in bacteria and mammals. Short-chain thioesters such as acetyl-CoA and succinyl-CoA are essential intermediates in carbon metabolism. CoA-thioesters of long chain fatty acids feed into β-oxidation and are also the source of fatty acids for phospholipids. In addition, CoA and its thioesters play important roles in the regulation of several enzymes in intermediary metabolism, including pyruvate dehydrogenase and phosphoenolpyruvate carboxylase. Finally,

synthesis of holo acyl carrier protein (ACP) is dependent on CoA for the 4'-
phosphopantetheine moiety linked to ACP. ACP is essential for fatty acid
biosynthesis. The two major acyl-carrier groups in cells: CoA and ACP, are derived
from pantothenate. Pantothenate can be obtained exogenously through uptake via a

5   permease, the product of the *panF* gene. Alternately, pantothenate is the product of
condensation of pantoate and β-alanine via pantothenate synthetase, the product of
the *panC* gene. The initial step in CoA biosynthesis is the phosphorylation of
pantothenate by pantothenate kinase (PanK, CoaA).

         The *coaA* gene was originally identified by Dunn and Snell in *S. typhimurium*

10   as a temperature sensitive allele. Similarly, a temperature sensitive allele of *coaA*
was reported for *E. coli* in 1987. CoaA was found to be essential in *E. coli* in a
recent genetic footprinting analysis. In the temperature sensitive strains,
accumulation of phosphorylated CoA intermediates rapidly ceased following shift to
the non-permissive temperature. CoaA was shown to be a homo-dimer of 35 kDa

15   subunits that bound ATP cooperatively. ATP is bound first in a sequential
mechanism of action; CoA has been shown to be a potent inhibitor of the reaction
and competitively competes for binding with ATP. Therefore CoaA is under feedback
regulation and is the major regulatory step in CoA biosynthesis.

         . Lysine 101 in bacterial pantothenate kinase (CoaA) was found to be essential

20   for both ATP and CoA binding. This supports kinetic data that CoA is a competitive
inhibitor of ATP binding to CoaA and that both substrates bind to the same site.

         Homologues of *E. coli* CoaA have been identified in *B. subtilis, S. pyogenes,*
M. tuberculosis, H. influenzae and *V. cholerae*. Homologues have not been identified
in either the *S. cerevisiae* genome or in a mammalian expressed sequence tag

25   database. Calder *et al.* identified a homologue, through functional complementation
of an *E. coli coaA* ts mutant, in *A. nidulans*. Homologue of this gene identified in
Alloiococcus otitidis as described in Example 5 (Seq. ID No 47. The protein encoded
by the gene is set forth in Seq. ID No. 48.

         The *A. nidulans* gene was then used to identify a yeast homologue. The

30   bacterial and Aspergillus enzymes were found to be 16% identical and 32% similar.
Although this level of similarity is quite weak the essential lysine residue involved in
nucleotide binding appears to be conserved; however, the sequence surrounding the
lysine residue were not conserved and further study will be required to validate this

finding. The most striking difference between the eukaryotic and prokaryotic enzymes is found in the sensitivity of each to competitive inhibition by CoA and acetyl-CoA. The yeast enzyme was most sensitive to acetyl-CoA and less sensitive to CoA, whereas the converse was true for the bacterial enzyme. Later studies

5 demonstrated that mammalian pantothenate kinase is activated by CoA and inhibited by acetyl-CoA.

Nucleotide binding

Binding of ATP to CoaA is directly demonstrated by equilibrium dialysis

10 employing the non-hydrolyzable ATP analogue ATPγS. The K_d measured for ATP binding is reported to be 2.1 µM.

CoA binding

Binding of CoA to CoaA is directtyl demonstrated by equilibrium dialysis and

15 the K_d is reported to be 6.7 µM.

Pantothenate kinase activity

Specific kinase activity of CoaA is demonstrated using D-[1-^{14}C]pantothenate and capturing 4'-phospho[1-^{14}C]pantothenate on DE81 filters. Using this assay the

20 following kinetic values were derived: specific activity – 470+/- 200 nmol/min/mg; pantothenate K_m – 36 µM; K_m ATP – 136 µM.

Suitability of target for anti-infective development

Coenzyme A biosynthesis is essential for bacterial viability. CoaA catalyzes the

25 first step of biosynthesis of CoA and appears to be the point of regulation for the pathway. The essentiality of CoaA is demonstrated through the construction of temperature sensitive alleles in coaA. Although the yeast enzyme is found to functionally complement the bacterial temperature sensitive allele, sequence and kinetic differences suggest the possibility of identifying inhibitors of the bacterial

30 enzyme with high selectivity. As CoaA is essential and conserved in gram-negative and gram-positive pathogens, such inhibitors will have broad-spectrum utility.

Suitable assays for measuring CoaA function

CoaA is purified by standard methods using widely available molecular tags following expression at high level from *E. coli*. Pantothenate kinase activity is measured as follows: CoaA and D-[1-^{14}C]pantothenate is incubated in a buffer

5   consisting of 100 mM Tris (pH 7.4), 2.5 mM MgCl$_2$, 2.5 mM ATP for 5-60 minutes at 37°C. Product, 4'-phospho[1-^{14}C] pantothenate, is monitored through retention of labeled material on DE81 filters. This assay is amenable to high-throughput screening using high-density well-filter plates.

10   EXAMPLE 7

IDENTIFICATION OF THE GENE ENCODING COABC (DFP) IN *ALLOIOCOCCUS OTITIDIS*

The *E. coli dfp* gene, which encodes the previously designated Dfp protein, was originally identified as encoding an enzyme required for CoA biosynthesis. The

15   gene, coding for the protein of interest, was renamed *coaBC* to reflect the enzyme function in CoA biosynthesis. CoA is an essential co-factor in a number of metabolic pathways in bacteria and mammals. Short-chain thioesters such as acetyl-CoA and succinyl-CoA are essential intermediates in carbon metabolism.

CoaBC carries out the second and third steps of coenzyme A

20   biosynthesis: the conjugation of 4'-phosphopantetheate with cysteine by the CoaB (PPCS : 4'phosphopantethenoyl cysteine synthase) activity followed by the conversion to 4'-phosphopantetheine by the CoaC (PPCDC: 4'phosphopantenoylcysteine decarboxylase) activity. Homologue of this gene identified in *Alloiococcus otitidis* as described in Example 5 (Seq. ID No 77). The

25   protein encoded by the gene is set forth in Seq. ID No. 78.

Enzyme activity of CoaBC (Dfp):

Initially it was demonstrated that Dfp enzyme catalyzing oxidative

30   decarboxylation of (R)-4'-phospho-N-pantothenoylcysteine (*PPC*) to form 4'-phosphopantetheine (*PP*) – the third step in CoA biosynthesis from pantothenate The K_M for this reaction is 800 μM for *PPC*.

Subsequently, it was established that Dfp is a bifunctional enzyme, catalyzing the second step of CoA biosynthesis, coupling of 4'-phosphopantothenate with

-80-

cysteine to form PPC, as well. This reaction is a two-step process and requires CTP for initial 4'-phosphopantothenate activation. Second step couples cysteine to the phosphopantothenate moiety with a release of CMP. Estimated K_M's are 300 μM for 4'-phosphopantothenate and CTP, and 250 μM for cysteine.

5

CoaBC as target for antibacterial development.

Coenzyme A (CoA) plays a vital role in the metabolism of living cells. According to a recent report, 4% of all enzymes in the cell require CoA, its thioesters
10   or 4'-phosphopantetheine. Recent genetic footprinting experiments on E. coli and direct gene knockout have established that this coaBC is essential for bacterial growth. Homologs of coaBC have been identified in a number of gram-positive and gram-negative organisms, which suggested the possibility of developing a broad-spectrum antibacterials from coaBC inhibitors. Considering the bifunctional nature of
15   CoaBC, it is feasible to identify inhibitors that will inhibit both enzymic functions, thus arresting two steps in the CoA pathway. Another important factor in favor of selecting CoaBC as a target for antibacterials is low homology of the bacterial enzyme to eukaryotic counterparts. In most of the higher organisms including humans, two separate enzymes carry out these functions. Moreover, mammalian
20   (R)-4'-phospho-N-pantothenoylcysteine decarboxylase is a pyruvate-dependent enzyme, while CoaBC requires flavine mononucleotide for its function.

Assays for measuring CoaBC activity.

25   PPC synthetase activity is be monitored by detecting the released pyrophosphate. This is achieved by converting pyrophosphate to inorganic phospate with pyrophosphatase and detection by the Malachite Green assay, or by the MESG assay spectrophotometrically. CoaBC (2 μg) is incubated in the reaction buffer containing 10 mM DTT, 2 mM $MgCl_2$, 50 mM Tris-HCl, pH 8, 300 μM 4'-
30   phosphopantothenate, 3.5 mM CTP, 5 μg pyrophosphatase. The reaction is started by addition of appropriate amount (10-500 μM final) of cysteine. The reaction is stopped at different time points by addition of equal volume of 5M H_2SO_4. The

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amount of inorganic phosphate released will be determined according to the one of described techniques.

PPC synthetase activity is also monitored by detecting the release of carbon dioxide from ^{14}C-labeled cysteine. CoaBC (2 µg) is incubated in the reaction buffer
5   containing 10 mM DTT, 2 mM MgCl$_2$, 50 mM Tris-HCl, pH 8, 2.5 µM 4'-phosphopantothenate, 3.5 mM CTP. The reaction is started by addition of appropriate amount (30 mM, final concentration) of ^{14}C-labeled cysteine. The reaction is stopped at different time points by addition of equal volume of 5M H$_2$SO$_4$. Amount of released ^{14}C-labeled CO$_2$ is determined according to published technique.
10

Example 8

Identification of the gene encoding phosphopantetheine adenylyltransferase
15   (CoaD) in *Alloiococcus otitidis*

Phosphopantetheine adenylyltransferase, (PPAT, CoaD, KdtB) catalyzes the penultimate step in Coenzyme A (CoA) biosynthesis. The fourth step in CoA
20   biosynthesis is the addition of AMP to 4'-phosphopantetheine by phosphopantetheine adenylyltransferase (CoaD) to form 3' dephospho-CoA (dPCoA).

The *coaD* gene was first identified in *E. coli* by Geerlof *et al.* CoaD is essential for viability in *E. coli* and *S. aureus*. The enzyme has a mass of 18 kDa and was determined to be a hexamer through cross-linking studies. Crystallography
25   confirmed the oligomeric state of the enzyme. Moreover, co-crystallography of CoaD with dPCoA has also been carried out mapping the binding pocket for the major product of the reaction. Interestingly, in mammals PPAT has been shown to be in a complex with dephospho Coenzyme A kinase (dPCoA kinase, DPCK). This enzyme, purified from pig liver, is referred to as CoA Synthase. The yeast PPAT is associated
30   with a protein complex that is in excess of 375 kDa and composed of six proteins. There is no detectable homology between the bacterial PPAT (CoaD) and the recently identified human PPAT, the activity of which is contained in a bifunctional PPAT/DPCK enzyme. Homologues of *E. coli* CoaD have been identified in *P. aeruginosa, S. pneumoniae, S. aureus, H. influenzae, H. pylori, B. anthracis* and *M.*
35   *tuberculosis*. Homologue of this gene identified in *Alloiococcus otitidis* as described in

Example 5 (Seq. ID No 81). The protein encoded by the gene is set forth in Seq. ID No. 82.

Enzyme activity

5   CoaD (PPAT) carries out the reversible transfer of AMP to 4'-phosphopantetheine, forming dephosphocoenzyme A and releasing PPi. The reverse reaction was demonstrated by Geerlof *et al.* using a coupled assay to tie ATP production to NADP reduction, which is monitored at 340 nm. The following kinetic constants were calculated: $k_{cat} = 3.3$ +/- 0.1 /sec; $K_{m(dPCoA)} = 7.0$ +/- 1.4 uM;

10     $K_{m(PPi)} = 0.22$ +/- 0.04 mM.

CoaD as target for anti-infective development.

       Coenzyme A biosynthesis is essential for bacterial viability. CoaD,

15   phosphopantetheine adenylyltransferase, catalyzes the fourth step in the pathway and was shown to be essential in both *E. coli* and *S. aureus*. There is no measurable homology between CoaD and the human PPAT enzyme, so the liability of poorly selective compounds is quite low. As CoaD is essential and conserved in gram-negative and gram-positive pathogens, inhibitors developed against this target will

20   have broad-spectrum utility.

Assays for measuring CoaD function

       CoaD will be expressed and purified using standard methodologies for bacterial expression and affinity tag-based purification. Two assay formats can be

25   used to monitor enzymatic activity: the forward reaction and the reverse reaction.

       The forward reaction assay was initially described for measuring the activity of the human PPAT activity in the PPAT/DPCK enzyme. The enzyme assay is carried out in 50 mM Tris (pH 8.0), 2 mM $MgCl_2$, 5 mM ATP, 5-500 uM 4'-phosphopantotheine, 7.5 mM NADH and enzyme (initially 0.1 – 1.0 µg/ml). The

30   production of PP_i is detected using the protocol of O'Brien in which PP_i production is coupled to the oxidation of NADH to NAD. This system requires the addition of 4 enzymes (PP_i-dependent phosphofructokinase, aldolase, triosephophate isomerase and glycerol-3-P dehydrogenase) to the basic reaction mix and presents the added issue of deconvolution, which limits the use of the assay as a primary screen.

The reverse direction assay is carried out also as a coupled assay to tie ATP production to NADP reduction following the method described by Lamprecht & Trautschold. The assay is set up in reaction buffer containing the following: 50 mM Tris (pH 8.0), 1 mM DTT, 2 mM $MgCl_2$, 1 mM NADP, 5 mM glucose, 2 mM PP_i, 0.1 mM dPCoA. Hexokinase (4 units) and glucose-6-phosphate dehydrogenase (1 unit) will be added to the assay as the coupling enzymes in addition to CoaD (initially 0.1 – 1 μg/ml). The assay is monitored at 340 nm. Deconvolution of hits is required with this assay, however with only 2 additional enzymes the task will be less cumbersome when compared to the forward assay described above.

Example 9

IDENTIFICATION OF THE GENE ENCODING DEPHOSPHOCOA KINASE (DPCK, YACE, COAE) IN *ALLOIOCOCCUS OTITIDIS*

DephosphoCoA kinase (DPCK, YacE, CoaE) encoded by the *coaE* gene catalyzes the final step in Coenzyme A (CoA) biosynthesis. The final step in CoA biosynthesis is the phosphorylation of the 3'-hydroxyl group of dephospho-CoA to form CoA by dephosphocoenzyme A kinase (DPCK, YacE, CoaE).

The determination that the previously identified *yacE* gene encoded the dephosphocoenzyme A kinase activity was reported by Mishra *et al.* These authors previously determined that separate enzymes encode the phosphopantetheine adenyltransferase (PPAT) and dephosphocoenzyme A kinase (DPCK) activity in *Corynebacterium ammoniagenes* in contrast to the eukaryotic enzymes in which the PPAT and DPCK activities are coupled. The *E. coli* gene, encoding a 25 kDa protein, was cloned based on the sequence of the *C. ammoniagenes* gene and found to be identical to the previously described *yacE* gene. The gene was designated *coaE* to follow existing nomenclature in *E. coli*. CoaE *(YacE)* was shown to be essential in *E. coli* through genetic footprinting. CoaE is widely distributed in bacteria. Homologue of this gene identified in *Alloiococcus otitidis* as described in Example 5 (Seq. ID No 93). The protein encoded by the gene is set forth in Seq. ID No. 94.

Assays for measuring CoaE function

CoaE carries out the phosphorylation of dephosphocoenzyme A at the 3'
hydroxyl group, consuming ATP, to form CoA. Dephosphocoenzyme A kinase
activity is measured in a coupled reaction in which NADH oxidation to NAD is tied to
5   ADP production. In this assay, the standard pyruvate kinase/lactose dehydrogenase
coupling system is used to generate NAD in a 1:1 molar equivalent to the ADP
produced by the test enzyme. NADH oxidation to NAD is monitored at 340 nm in a
standard spectrophotometer. The following kinetic values were determined for CoaE:
$K_{m (ATP)}$ = 0.74 mM; $K_{m (dephospho-CoA)}$ = 0.14 mM (7).

10   The formation of CoA is monitored using a coupled enzyme system in which
acetyl-CoA is formed in proportion to the amount of CoA in the assay. Three
enzymes (phosphate acetyl transferase, citrate synthase and malate dehydrogenase)
are added to the reaction that results in the formation of NADH from NAD, which is
monitored at 340 nm.

15

CoaE as a target for anti-infective development

Coenzyme A biosynthesis is essential for bacterial viability. CoaE,
dephosphocoenzyme A kinase, catalyzes the final step in CoA synthesis and is
shown to be essential by genetic footprinting in *E. coli*. A degree of homology
20   between CoaE and the human DPCK enzyme has been noted, such that selectivity
assays is necessary to determine a high therapeutic index for CoaE inhibitory
compounds. CoaE is conserved in gram-negative and gram-positive pathogens and
should have broad-spectrum utility in the clinic.

CoaE is expressed and purified using standard methodologies for bacterial
25   expression and affinity tag-based purification. DephosphocoA kinase activity is
monitored using a coupled enzyme system to tie ADP production to oxidation of
NADH to NAD. The decay of absorbance at 340 nm will be the assay readout. The
assay will be setup in the following buffer: 50 mM Tris (pH 8.5), 20 mM KCl, 10 mM
$MgCl_2$, 10 mM ATP, 0.3 mM NADH and 0.4 mM phosphoenolpyruvate. The coupling
30   enzymes: pyruvate kinase (10 U) and lactate dehydrogenase (4 U) will be added
along with dephosphocoenzyme A kinase (initially 0.1- 1.0 ug/ml). The assay will be
started by the addition of 0.4 mM dephosphocoenzyme A. In this assay system, the
release of ADP is tied to the oxidation of NADH to NAD, and is monitored at 340 nm.

This assay is transferable to a high-density microtiter plate format and suitable for HTS.

EXAMPLE 10

IDENTIFICATION OF DNAB AND PCRA, GENES ENCODING HELICASES IN *ALLOIOCOCCUS OTITIDIS*

Helicases unwind double-stranded DNA in a reaction that couple nucleotide binding and hydrolysis to strand unwinding. Their activity is required for a number of biological processes such as separation of the chromosome during replication, recombination and repair. Homologue of thse genes were identified in *Alloiococcus otitidis* as described in Example 5 (Seq. ID No 15 and 99). The protein encoded by the gene is set forth in Seq. ID No. 16 and 100.

Due to the essential roles modulated by these molecules they represent an important target for antibacterial therapy. Homologs of *dnaB* and *pcrA* genes encoding helicases were identified as described in Example 5. A primary assay, which detects helicase function *in vitro*, is used to identify inhibitors of each enzyme and is described below.

Genes encoding DnaB and PcrA is obtained using polymerase chain reaction amplification of the genomic region encoding them. The genes is subcloned into a standard expression vector either containing an amino acid tag for ease of purification or not. The enzyme is then over-expressed in *Escherichia coli* and purified using a standard tag system.

Most helicases require a region of single-stranded DNA flanking the duplex region that it unwinds. As a result, providing a single stranded region to either the 3' or 5' end of a duplex allows for determination of the polarity of helicase unwinding. These types of experiments have demonstrated that PcrA and DnaB are 3'-5' and 5'-3' helicases, respectively. None the less, a convenient filtration assay has previously been described that is formatted for high-through-put screening of inhibitors of either enzyme, regardless of polarity. Assays (90 ul) contained 15 pM single-stranded M13 DNA to which a radiolabeled oligonucleotide had been annealed as a substrate for unwinding. Reactions are carried out in 96-well GF/C unifilter hydrophobic plates (Polyfiltronics Inc.) in 70 ul helicase buffer [20 mM Hepes (pH 7.6), 4 mM MgCl₂ 4

mM ATP, 100 ug/ml BSA, 5% glycerol and 2 mM DTT] and 10 ul of DMSO or

compound. Reactions are initiated by adding 10 ul of purified helicase protein and

are incubated for 1 hr at room temperature. 100 ul of 2X capture buffer containing

silica beads [25% methanol, 3 M Nal, 0.03% NP-40, and 10% GlassFog beads

5   (BIO101)] were added. The mixture was incubated for 30 min at room temperature.

Plates are then washed 5X on a Bio-Teck instruments, Auto Washer EL403) with

wash buffer (50% ethanol, 0.2% NP-40 and 50 mM NaCl). Scintillation fluid was

added and plates are counted (Packard Topcount).

10   EXAMPLE 11

IDENTIFICATION OF DNAE, THE GENE ENCODING DNAE-POLYMERASE IN *ALLOIOCOCCUS
OTITIDIS*

         DnaE is an enzyme that catalyzes the DNA template directed polymerization

15 of deoxyribonucleotides into deoxyribonucleic acid. The enzyme has been reported

to modulate lagging strand synthesis at gram-positive replication forks. Functions for

DnaE have been defined biochemically, in *Bacillus subtilis* and *Streptococcus*

pyogenes. Homologue of this gene identified in *Alloiococcus otitidis* as described in

Example 5 (Seq. ID No 75). The protein encoded by the gene is set forth in Seq. ID

20 No. 76.

         Because DnaE is an essential protein in gram-positive bacteria and has high

homology to the gram-negative *dnaE*, which is an essential polymerase subunit of

the DNA polymerase III holoenzyme, it serves as a good target for antibacterial drug

discovery. A primary assay, which detects processive DnaE mediated DNA

25 synthesis *in vitro*, is useful identify inhibitors of the enzyme and is described below.

         The gene encoding DnaE I in *Alloiococcus otitidis* was identified as described

in Example 5. Purification of DnaE DNA polymerase from *Alloiococcus*. The gene

encoding DnaE is obtained using polymerase chain reaction amplification of the

dnaE gene. The gene is subcloned into a standard expression vector either

30 containing an amino acid tag for ease of purification or not. The enzyme is then

over-expressed in *Escherichia coli* and purified using a standard tag system.

         Because DnaE catalyzes the incorporation of single deoxyribonucleotides into

DNA, the incorporation of radiolabelled deoxyribonucleotides into larger

deoxyribonucleic acid molecules is monitored to measure activity of the enzyme. A

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filtration assay has been previously described for *Streptococcus pyogenes* DnaE that uses filterplates containing DE81 filters to capture polymerized DNA. This assay is amenable to high-through-put screening format for DnaE. Assays contained 70 ng of 30-mer primed M13mp18 single stranded DNA as a template for replication. The

5   reaction contained 3.3-300 ng of DnaE in 23.5 µl of replication buffer [20 mM Tris-HCL (pH 7.5), 4% glycerol, 0.1 mM EDTA, 5 mM DTT, 2 mM ATP, 8 mM MgCl$_2$, 40 µg/ml BSA] and 60 µM of both dGTP and dCTP. NaCl was added to the reaction mixture to a final concentration of 40 mM. DNA synthesis was initiated by the addition of 1.5 µl of 1.5 mM dATP and 0.5 mM [µ-^{32}P]dTTP. Reactions were

10   incubated at 37°C for various lengths of time and were quenched by adding an equal volume of 1% SDS and 40 mM EDTA. One-half of the terminated reaction was applied to DE81 filter paper and washed 3X with wash solution (0.3 M Ammonium formate and 0.01 M Sodium pyrophosphate). Filters were then placed in scintillation vials and 1 ml scintillation counting liquid was added. Radioactivity was counted

15   using a scintillation counter.

EXAMPLE 12

IDENTIFICATION OF DNAG, THE GENE ENCODING PRIMASE IN *ALLOIOCOCCUS OTITIDIS*

20   DnaG is an enzyme that catalyzes the DNA template directed polymerization of ribonucleotides into ribonucleic acid *de novo*. Ribonucleic acid molecules that are synthesized by DnaG primase subsequently serve as primers for synthesis of the leading- and lagging-strands during chromosomal replication. Functions for DnaG have been defined biochemically, and the crystal structure of the RNA polymerase

25   domain has been determined in *Escherichia coli*. Homologue of this gene identified in *Alloiococcus otitidis* as described in Example 5 (Seq. ID No 63). The protein encoded by the gene is set forth in Seq. ID No. 64.

Because DnaG primase plays an essential role in both leading- and lagging-strand synthesis during chromosomal replication, and DnaG has homologs in all

30   prokaryotes but not eukaryotes, it serves as a good target for antibacterial drug discovery. A primary assay, which detects DnaG mediated RNA synthesis *in vitro*, can be used to identify inhibitors of the enzyme and is described below.

Assay for the activity of DNA polymerase and identification of compounds that inhibit DnaG

The gene encoding DnaG is obtained using polymerase chain reaction
5   amplification of the *dnaG* gene. The gene is subcloned into a standard expression vector either containing an amino acid tag for ease of purification or not. The enzyme is then over-expressed in *Escherichia coli* and purified using a standard tag system.

Because DnaG catalyzes the incorporation of single ribonucleotides into RNA,
10   the incorporation of radiolabelled ribonucleotides into larger ribonucleic acid molecules is monitored to measure activity of the enzyme. A high-throughput scintillation proximity assay (SPA) assay, previously described for *E. coli* DnaG, is used to meadure activity of DnaG activity in a coupled reaction with DnaB helicase. The assay, which was shown to work with DnaG alone, is used to screen for
15   compounds that inhibit DnaG function. Assays are run in 96-well Packard Optiplate plates. First, 1 µl DMSO or test compound was added, followed by 20 µl of DnaG (208 nM) and 3.3 nM M13mp18 single-stranded DNA. Reactions are initiated by adding 10 ul of primase assay buffer [50 mM Tris-HCl (pH 7.5), 4% sucrose, 8 mM DTT, 5 mM MgCl$_2$, 40 ug/ml BSA, 0.1 µg/ul Rifampicin, 25 U/ml RNA guard, 100 µM
20   GTP, 100 µM UTP, 3 µM CTP, 1 mM ATP] and 0.4 µCi [^{3}H]CTP. Reactions are incubated at 30°C for 30 min. Next, a suspension of 50 µl of 2.5 mg/ml PVT-PEI SPA beads (Amersham; prepared in 0.3 M NaCitrate, pH 3.0) were added. Plates were read after 1 hr on a Topcount instrument (Packard).

25   EXAMPLE 13

DNAN, DNAX, HOLA, HOLB, AND POLC, THE GENES ENCODING THE SUBUNITS OF *ALLOIOCOCCUS OTITIDIS* DNA POLYMERASE III HOLOENZYME: BETA (β), TAU (τ), DELTA (Δ), DELTA' (Δ') AND POLC.
30

DNA polymerase III holoenzyme is an enzyme complex comprised of multiple highly conserved subunits that catalyzes the DNA template directed polymerization of deoxyribonucleotides into deoxyribonucleic acid. In gram positive organisms the holoenzyme is composed of a polymerase subunit, PolC, and accessory proteins.
35   The accessory proteins act in a coordinated manner to clamp the polymerase tightly to the DNA template allowing the polymerase to synthesize DNA with high speed and

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processivity. Homologue of these genes identified in *Alloiococcus otitidis* are described in Example 5 (Seq. ID Nos. 21, 105, 79, 103, and 105 respectively). The protein encoded by the gene is set forth in Seq. ID No. 22, 106, 80, 104 and 106 respectively).

5   Functions for the individual subunits have been defined biochemically and interactions between them have now been deduced structurally by crystallographic analysis of the enzyme from *Escherichia coli*. Tau interacts directly with both delta and delta' to form a clamp loader complex. Upon binding ATP the complex undergoes a conformational change altering an interaction between delta and delta',

10   which allows delta to subsequently interact with the beta-clamp. The beta-clamp is a ring-shaped homomultimer assembly that can be opened by delta and placed onto a primed DNA template. ATP hydrolysis results in closing the clamp around DNA and dissociation of the clamp-loading complex. PolC then couples with the beta clamp to form a highly processive polymerase.

15   Because DNA polymerase III holoenzyme is comprised of multiple subunits, the opportunity exists to inhibit its activity at a number of different sites. A primary assay, which detects processive DNA synthesis *in vitro*, can be used to identify inhibitors of the enzyme and is described below. Deconvolution of inhibitors, based on either activity of physical interaction, follow the primary assay.

20

Assay for the activity of DNA polymerase

Purification of DNA polymerase III holoenzyme subunits from *Alloiococcus*. Genes encoding the subunits of DNA polymerase is obtained using polymerase chain reaction (PCR) amplification of the genomic region encoding them. The genes

25   are subcloned into a standard expression vector either containing an amino acid tag for ease of purification or not. The enzyme is then over-expressed in *Escherichia* coli and purified using a standard tag system.

Because DNA polymerase III catalyzes the incorporation of single deoxyribonucleotides into DNA, the incorporation of radiolabeled deoxynucleotides

30   into larger deoxyribonucleic acid molecules is monitored to measure activity of the enzyme. A filtration assay is previously described for *Streptococcus pyogenes* DNA polymerase III that uses filterplates containing DE81 filters to capture polymerized DNA (2). This assay is amenable to high-through-put screening format. Assays

contained 70 ng of 30-mer primed M13mp18 single stranded DNA as a template for replication. The reaction contained 43 ng of ß and 140 ng of PolC-тдд' complex in 23.5 μl of replication buffer (20 mM Tris-HCL (pH 7.5), 4% glycerol, 0.1 mM EDTA, 5 mM DTT, 2 mM ATP, 8 mM $MgCl_2$, 40 μg/ml BSA, and 60 μM of both dGTP and ·

5   dCTP. DNA synthesis was initiated by the addition of 1.5 μl of dATP and [μl-^{32}P]dTTP. Reactions were incubated at 37°C for various lengths of time and were quenched by adding an equal volume of 1% SDS and 40 mM EDTA. One-half of the terminated reaction was applied to DE81 filter paper and washed 3X with wash solution (0.3 M Ammonium formate and 0.01 M Sodium pyrophosphate). Filters were

10   then placed in scintillation vials and 1 ml scintillation counting liquid was added. Radioactivity was counted using a scintillation counter.

       Compounds inhibiting PolC subunit is identified by modifying the above reaction to include only the PolC subunit and using 2.5 μg activated calf thymus DNA as a substrate, instead of singly-primed M13mp18 DNA, as previously described.

15   Several techniques are utilized to determine the interaction of inhibitors with individual subunits. These have been described in the literature and include the following: (1) Nuclear magnetic resonance and capillary electrophoresis.

20

EXAMPLE 14
ERA GTPASE IN ALLOIOCOCCUS OTITIDIS

       The era (E. coli Ras) gene was initially identified while sequencing around the

25   rnc gene; era lies downstream of rnc. While a function for era has yet to be determined, conditional (temperature sensitive) mutants revealed that the product of the era gene, Era, is essential for E. coli viability. A hint as to an in vivo function for Era was uncovered when a suppressor of a dnaG (primase) allele was found to map in the era coding sequence and a second suppressor, which mapped upstream of the

30   era open reading frame, affected expression of era. These data suggest that Era could play one or more roles in DNA replication, regulation of primase activity or otherwise effect cell cycle progression. More recent data has confirmed that the era1 mutant causes a defect in cell growth at the two-cell stage and delays cell division Moreover, Britton et al demonstrated that cell division was coupled with the level of

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Era in the cell: division arrest, through reduction in Era levels, is reversed when Era levels return to threshold amount. A current model suggests that Era acts as a checkpoint regulator in the bacterial cell cycle. Era is a GTP-binding protein with GTPase activity, a threshold level of functional/activated Era may be required to
5   initiate septation.

Era is associated with additional cellular functions, specifically translation, as Era specifically interacts with the translation machinery. *E. coli* Era binds both 16S rRNA and the 30S ribosomal subunit; whereas, the *S. pneumoniae* 16S rRNA co-purifies with Era. A putative RNA binding "KH motif" has been identified in the
10   carboxyl-terminal domain. The RNA binding activity is critical to Era cellular function as mutation of the putative RNA binding region of the *S. pneumoniae* Era prevents complementation of an *E. coli era* mutant strain. Homologue of this gene identified in *Alloiococcus otitidis* as described in Example 5 (Seq. ID No 65). The protein encoded by the gene is set forth in Seq. ID No. 66.

15

Nucleotide binding

Filter-binding assays are utilized to demonstrate nucleotide-binding specific to GTP and not UTP, CTP or ATP. Both GTP and GDP (unlabeled) were capable of inhibiting $\alpha^{32}P$-GTP binding. The Kd for GTP and GDP binding were reported to be
20   5.5 and 1.0 µM, respectively.

A large number of GTP-binding proteins have been studied and all members of the family contain three regions of highly homologous amino acid residues that define a GTP-binding pocket. Era contains well-conserved regions defining the so-called G1 (G/AXXXXGKT/S: residues 15-22), G3 (DXXG: residues 62-65) and G4
25   (NKXD: residues 124-128) consensus sequences. The G2 domain (residues 33-38, see below), located between G1 and G3, is generally more variable.

GTPase activity

Purified Era showed a significant GTPase activity, which is inhibitable by GTP
30   or GDP but not by UTP, CTP, ATP or ADP. The maximum hydrolysis rate is measured at 9.8 mmol GTP hydrolyzed/min/mol Era. The Km was found to be 9 µM.

It should be noted that Sullivan *et al* demonstrated, using mant (*N*-methyl-3'-O-anthraniloyl) labeled GTP and GDP, very rapid exchange kinetics for guanine

nucleotide binding. Era exchanges guanine nucleotides 10-fold more rapidly than the GTP hydrolysis rate suggesting that guanine nucleotide binding and release should be considered as a regulatory point in addition to the more well-studied hydrolysis step.

Autophosphorylation

When γ^{32}P-GTP is used as a substrate for the GTPase activity , Era is phosphorylated. The autophosphorylation reaction is specific for GTP, as incubation with γ^{32}P-ATP did not result in phosphorylation of Era. Moreover, α^{32}P-GTP is not a suitable substrate for detection of Era autophosphorylation. Tryptic digestion and HPLC were utilized to resolve the sites(s) of phosphorylation. Using γ^{32}P-GTP as a substrate the major radioactive peak contained the tryptic peptide, ISITSR, corresponding to Era residues 33-38 and containing 3 potential phosphorylation sites. Mutagenesis of both Thr-36 and Ser-37 to alanine abolished enzymatic activity. However, individual alanine substitutions at either site had no effect on Era function. The autophosphorylation site is located in the so-called G2 domain of Era.

Suitability of target for anti-infective development

Era is an essential protein for bacterial viability. Knock-down mutations as well as conditional-lethal alleles revealed that Era function is required for cytokinesis. An additional phenotype of the Era-depleted strains is an aberrant response to temperature induced stress. This target is novel and may well lead to the identification of new classes of anti-infectives. The widespread distribution of Era homologues in both gram-negative and gram-positive pathogens suggests that broad-spectrum agents could result from an effort to define Era inhibitory compounds.

Assays for measuring Era function

NUCLEOTIDE BINDING ASSAYS

Era binding to nucleotide is monitored by a simple filter-binding assay. Era (1-5 µg) is incubated with α^{32}P-GTP (0.2 µCi) in a buffer consisting of 100 mM Tris (pH 7.5), 10 mM MgCl$_2$, 0.2% NP-40, 0.2 mg/ml BSA for 30 minutes at 32°C. A

portion of the reaction mix is spotted on nitrocellulose membrane, washed (50 mM Tris (pH 7.5), 5 mM $MgCl_2$, 1 mM DTT) and dried. The membrane is then exposed to X-ray film. Alternatively, the spots are excised and counted. This assay is directly amenable to HTS using filter plates.

5

GTPASE ACTIVITY ASSAY

The GTP hydrolytic activity of Era is monitored using thin-layer chromatography. Era and α^{32}P-GTP is incubated in 50 mM Tris (pH 7.5), 5 mM MgCl2, 0.1% NP-40, 0.2 mg/ml BSA for 30 minutes at 37°C. An aliquot of the

10 reaction is placed on PEI cellulose and the strip developed with 0.5 M KH_2PO_4, 1.0 M NaCl (pH 3.7). The spots conforming to GDP and GTP are identified by UV shadowing, excised and counted. This assay represents an acceptable secondary/confirmatory assay.

Alternatively, the hydrolysis of γ^{32}P-GTP is monitored by assaying for

15 liberated P_i. Obg and α^{32}P-GTP is incubated in 50 mM Tris (pH 8.5), 1.5 mM $MgCl_2$, 0.1 mM EDTA, 100 mM KCl, 10% glycerol for 30 minutes to 3 hours at 37°C. The reaction will be stopped by the addition of a slurry of charcoal in 1 mM Kpi (pH 7.5), which selectively binds the GTP and GDP. The liberated P_i in the supernatant is monitored by Cerenkov counting. Free P_i can also be monitored with the Malachite

20 Green reagent.

AUTOPHOSPHORYLATION ASSAY

Era autophosphorylation is monitored by incubating Era with γ^{32}P-GTP in 50 mM morpholinopropane sulphate (pH 6.8), 5 mM MgCl2, 1 mM DTT at 37°C (14).

25 Samples are analyzed following separation on SDS polyacrylamide gels, drying the gel and exposure to film. This assay represents an acceptable secondary/confirmatory assay for Era activity.

EXAMPLE 15
FMHB(FEMX) GENES IN ALLOIOCOCCUS OTITIDIS

5   The *femA*, *femB*, and *fmhB(femX)* genes have been shown to be essential for incorporation of glycine into the side chain of peptidoglycan precursors in *Staphylococcus aureus,*. The *femAB* locus was initially identified as a factor essential for methicillin resistance (*fem*) based on random insertional inactivation of chromosomal genes and a screen for reduced expression of resistance mediated by

10   the penicillin binding protein 2A (PBP2A). Inactivation of *femA* or *femB* was subsequently reported to prevent incorporation of glycine residues at positions 2 to 5 or positions 4 to 5 of the penta-glycine cross bridge since muropeptides cross-linked by one or three glycine residues were detected in the corresponding mutants. Inactivation of *fmhB*, formerly *femX*, is lethal, but the construction of a mutant

15   conditionally expressing *fmhB* under the control of a xylose-inducible promoter showed that the gene was essential for synthesis of branched peptidoglycan precursors . These studies show that the *fem* gene products were required for incorporation of glycine at positions 1 (FmhB), 2 and 3 (FemA), and 4 and 5 (FemB) of the cross bridge, although the catalytic activity of the proteins has not been directly

20   assessed. Similarly, inactivation of two *fmhB* homologues in *Streptococcus pneumoniae*, designated *murM* (*fibA*) and *murN* (*fibB*), reduced addition of L-Ala or L-Ser to the -amino group of L-Lys and subsequent addition of a second L-Ala residue, respectively. Overall, disruption of the *murMN* operon reduced the proportion of branched peptide stems in the peptidoglycan from 89 to 33% . In contrast to what

25   occurs in *S. aureus*, direct cross-linking of L-Lys to D-Ala occurs in *S. pneumoniae*, and the *murMN* operon was accordingly reported to be unessential.

          BLAST analysis of *Alloiococcus otitis* genome revealed an ORF similar to *femX* of *Weissella viridescent* , and *fmhB* of *S. aureus*. It suggests that in *Alloiococcus otitis* there is an enzyme with similar to FhmB function. Homologue of

30   this gene identified in *Alloiococcus otitidis* is described in Example 5 /Table 4 (Seq. ID No 97). The protein encoded by the gene is set forth in Seq. ID No. 98.

Assays for measuring FmhB function

There are no *in vitro* biochemical assays to test enzymatic activity of *S. aureus* FmhB because the reaction occurs at the membrane-bound lipid II precursor GlcNAc-(β-1,4)-*N*- acetylmuramic acid(-L-Ala-D-iGln-L-Lys-D-Ala-D-Ala)-

5   pyrophosphoryl-undecaprenol.

Lipid II is a minor component of bacterial cell membrane which is detected by thin-layer chromatography separation of presolubilized membranes supplied with the cytoplasmic precursors, UDP-*N*-acetylmuramyl-pentapeptide (UDP-MurNAc-pentapeptide) and [^{14}C]UDP-*N*-acetylglucosamine ([^{14}C]UDP-GlcNAc).

10   The *in vitro* biosynthesis of branched lipid II of *S. aureus* requires whole-cell membranes, cytoplasmic PG precursors, glycine (^{14}C labeled for detection of reaction products), purified tRNA, and an intracellular fraction that contains tRNA-activating enzymes. Therefore, the *in vitro* assay of *S. aureus* FmhB is a tedious procedure.

One way to facilitate this procedure is to use *Weissella viridescens* FemX or

15   *E. faecalis* UDP-MurNac-pentapetide:L-alanine ligase. Recombinant *Weissella viridescens* FemX *and E. faecalis* UDP-MurNac-pentapetide:L-alanine ligase were purified, and their *in vitro* activity was demonstrated. The distinctive feature of these enzymes is that they catalyze the addition of a branching amino acid (Ala) to the cytoplasmic cell wall precursor UDP-MurNac-pentapetide.

20   Other bacteria for which the biosynthesis of Gly-containing branched UDP-MurNac-hexapeptide in cytoplasm was shown are *Streptomyces lividans* and *Streptomyces hydroscopicus*, although the enzymes were not isolated and their ligase activity remain to be demonstrated.

These new data open an opportunity to develop an assay to detect the

25   activity of FmhB(FemX) by using cytoplasmic UDP-MurNac-pentapetide. Products of the reaction are detected by HPLC. HPLC separation of precursors are performed by the method of Flouret et al. The precursors are separated by reverse-phase HPLC on a μBondapak C_{18} column (3.9 by 300 mm; Waters) in 50 mM ammonium formate (pH 3.9) at a flow rate of 0.5 ml/min. The elution of precursors is

30   monitored at a wavelength of 254 nm.

EXAMPLE 16

FOLA- DIHYDROFOLATE REDUCTASE (DHFR)

5   The *Alloiococcus* ORF-1863 encodes a homolog of *S. aureus* dihydrofolate reductase that catalyzes the NADPH-dependent conversion of dihydrofolate to tetrahydrofolate, one of the steps in bacterial folate biosynthesis. Homologue of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 55). The protein encoded by the gene is set forth in Seq. ID No. 56.

10

FOLA as a target for anti-infective development

        Folate is an essential cofactor in many important metabolic processes in bacteria, such as purine, pyrimidine, amino acid and pantothenate biosynthesis. Unlike mammalian cells, bacteria are unable to utilize exogenous folate derivatives, and

15   therefore must synthesize folate *de novo*. Bacterial folate biosynthesis occurs via two converging pathways, the non-essential para-amino-benzoate (PABA) synthesis pathway, and synthesis of the pterin precursor, to which pABA is subsequently attached to form the folate precursor. Bacterial DHFRs are essential for viability and well conserved across all bacterial species. Although bacterial DHFR shares

20   similarity with human DHFR, selective inhibitors against bacterial DHFR have been identified in the past such as trimethoprim which specifically blocks the bacterial DHFR step. Thus DHFR still remains an attractive target for development of broad-spectrum antibacterial agents.

25 **Assays for measuring DHFR activity**

        DHFR activity is monitored spectrophotometrically, recording the change of absorbance at 340 nm due to the equimolar consumption of NADPH in the course of dihydrofolate substrate reduction. DHFR (10 ng) is preincubated in reaction buffer containing 50 mM 2-(N-morpholino)ethanesulfonic acid, 25 mM Tris-HCl, 25 mM

30   ethanolamine, and 100 mM NaCl at pH 7.5 for 3 minutes. The reaction is started by   ,
addition of 0.5-10 μM 7,8-dihydrofolate. The amount of processed substrate is calculated from the decrease of absorbance at 340 nm due to oxidation of NADPH ($\square=11800$ M^{-1}cm^{-1}) to NADP$^+$.

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EXAMPLE 17

FOLB- DIHYDRONEOPTERIN ALDOLASE (DHNA)

5   The *Alloiococcus otitidis* ORF-959 encodes a homolog of *S. aureus*
dihydroneopterin aldolase that catalyzes the conversion of 7,8-dihydroneopterin to 6-
hydroxymethyl-7,8-dihydropterin, one of the early steps in bacterial folate
biosynthesis. Homologue of this gene identified in *Alloiococcus otitidis* is described in
Example 5/Table 4 (Seq. ID No 31). The protein encoded by the gene is set forth in
10   Seq. ID No. 32.

FOLB as a target for anti-infective development

Folate is an essential cofactor in many important metabolic processes in
bacteria, such as purine, pyrimidine, amino acid and pantothenate biosynthesis.
15   Unlike mammalian cells, bacteria are unable to utilize exogenous folate derivatives,
and therefore must synthesize folate *de novo*. Bacterial folate biosynthesis occurs via
two converging pathways, the non-essential para-amino-benzoate (*p*ABA) synthesis
pathway, and synthesis of the pterin precursor, to which *p*ABA is subsequently
attached to form the folate precursor. Enzymes that catalyze steps in the folate
20   biosynthesis pathway are essential and well conserved across all bacterial species,
and those that act in early steps such as FolB have no direct homologs in mammals.
Thus FolB becomes an attractive target for development of broad-spectrum
antibacterial agents.

25   **Assays for measuring FOLB activity**

FolB (DHNA) 7,8-dihydroneopterin aldolase activity is monitored individually
or in conjunction with downstream enzymes in folic acid biosynthesis pathway (FolK
and Sul).

FolB activity is monitored directly by HPLC assay. FolB substrate (7,8-
30   dihydro-D-neopterin) is commercially available from Schircks Laboratories
(Swizerland). FolB (0.5 µg) is preincubated in reaction buffer containing 50 mM Tris-
HCl (pH 8.0), 50 mM KCl, 0.1 mg/ml BSA, 2.5 mM dithiothrietol for 5 min. Reaction
is started by addition of stock solution of 7,8-dihydro-D-neopterin in DMSO (100 µM

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final concentration). Reaction is terminated by addition of 1/3 of reaction volume of 1% I_2, 2% KI in 1M HCl with subsequent incubation at room temperature for 5 minutes. Quenched reaction will be applied directly to HPLC. Oxidized starting material and reaction products are efficiently separated on ODS (C18) column.

5   Reaction components are detected and quantified by analysis of UV absorbance at 254 nm, or fluorescence (excitation at 365 nm; emission at 446 nm).

FolB activity are also monitored in the coupled assay with FolK (HPPK) and Sul (DHPS) enzymes. FolB activity is measured by detection of radioactive dihydropteroate formation as described in FolK and Sul assays, under conditions of

10   excess of the later enzymes. FolB enzyme and substrate 7,8-dihydro-D-neopterin are added to the described assay to replace the 6-hydroxymethyl-7,8-dihydropterin (FolK substrate).

EXAMPLE 18

15   ### FOLC- DIHYDROFOLATE SYNTHASE (DHFS)

The *Alloiococcus otitidis* ORF-956 and ORF-528 both encode a homolog of *B. subtilis* dihydrofolate synthase that catalyzes the conversion of 7,8-dihydropteroate and glutamate to dihydrofolate, one of the steps in bacterial folate biosynthesis [.

20   Homologue of this gene identified in *Alloiococcus otitidis* as described in Example 5 (Seq. ID Nos. 29 and 23). The protein encoded by the gene is set forth in Seq. ID Nos. 30 and 24.

Use of FoLC as a target for anti-infective development

25   Folate is an essential cofactor in many important metabolic processes in bacteria, such as purine, pyrimidine, amino acid and pantothenate biosynthesis. Unlike mammalian cells, bacteria are unable to utilize exogenous folate derivatives, and therefore must synthesize folate *de novo*. Bacterial folate biosynthesis occurs via two converging pathways, the non-essential para-amino-benzoate (*p*ABA) synthesis

30   pathway, and synthesis of the pterin precursor, to which *p*ABA is subsequently attached to form the folate precursor. Enzymes that catalyze steps in the folate biosynthesis pathway are essential, and are well conserved across all bacterial species. Bacterial FolC appears to be a bifunctional enzyme possessing both

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dihydrofolate synthase (DHFS) activity and folyl-polyglutamate synthetase (FPGS) activity, which are probably mediated through different sites of the protein. The bacterial DHFS activity but not the FPGS activity is essential for viability. Although bacterial FolC shares similarity with human FPGS, the human enzymes apparently

5   lack DHFS activity and display a folate substrate specificity quite distinct from that of bacterial enzymes. Thus targeting bacterial FolC/DHFS activity selectively might lead to identification of broad-spectrum antibacterial agents.

Assays for measuring FoLC activity

10   FolC (DHFS) 7,8-dihydrofolate synthase activity in the presence or absence of antimicrobial compounds or putative inhibitory compounds are monitored by several methods.

In one method, FolC activity is monitored directly by simple HPLC assay. FolC substrate (7,8-dihydropteroic acid) is commercially available form Schircks

15   Laboratories (Switzerland). FolC (15 ng) is added to reaction mix, containing 10 mM glutamate, 5 mM ATP, 50 mM Tris-HCl (pH 8.0), 20 mM Mg_2Cl, 50 mM KCl, 0.1 mg/ml BSA, 5 mM dithiothreitol. Reaction is started by addition of stock solution of 7,8-dihydropteroic acid in DMSO (10 μM final concentration). Reaction is terminated by addition of equal volume of 8M Guanidinium hydrochloride. Stopped reaction is

20   applied directly to HPLC. Starting material and reaction products are efficiently separated on ODS (C18) column. Reaction components are detected and quantified by analysis of UV absorbance at 254 nm, or fluorescence (excitation at 280 nm; emission at 420 nm).

In another method, the FolC activity monitoring is by detection of ADP

25   accumulation. ADP is released in the amount equimolar to the amount of the product formed. ADP detection is performed by coupling its conversion to ATP by pyruvate kinase in the presence of phospho(enol)pyruvate producing pyruvate. Lactate dehydrogenase reduces pyruvate to S-lactate in the presence of NADH. Course of reaction is monitored by decrease in absorbance at 340 nm due to oxidation of

30   NADH (ε=6220 $cm^{-1}M^{-1}$) to NAD^+. Reaction conditions are as following: 5 mM dithiothreitol, 5 mM ATP, 380 μM NADH, 10 mM glutamate, 2 mM phospho(enol)pyruvate, 50 mM KCl, 20 mM Mg_2Cl, 50 mM Tris-HCl, 50 μg of

pyruvate kinase, 50 µg of S-lactate dehydrogenase. Reaction is started by addition

7,8-dihydropteroic acid in DMSO (10 µM final concentration).

In yet another method, FolC activity is monitored through detection of

inorganic phospate release. Amount of inorganic phosphate in solution is quantified

5   by:

(i) its conversion by purinenucleoside phosphorylase leading to

phosphorylation of MESG. Later assay kit is available from Molecular Probes

as EnzCheck™ Phosphate Assay Kit;

(ii) its reaction with Malachite Green reagent; and

10   (iii) detecting the release of radioactive inorganic phosphate in reaction with γ-

^{33}P-labeled ATP following the absorption of unprocessed ATP by charcoal.

First method is applied in rate-based assay format; the later two in

end-point format. Reaction conditions are similar to the ones described in

HPLC-based assay.

15

EXAMPLE 19

FOLK- 6-HYDROXYMETHYL-7, 8-DIHYDROPTERIN PYROPHOSPHOKINASE (HPPK)

The Alloiococcus otitidis OFR-961 (Seq. ID No. 33) encodes a homolog of S.

20   aureus 6-hydroxymethyl-7,8-dihydropterin pyrophosphokinase that catalyzes

pyrophosphoryl transfer from ATP to 6-hydroxymethyl-7,8-dihydropterin, one of the

early steps in bacterial folate biosynthesis. The protein encoded by this ORF is set

forth in Seq. ID No. 34. (see Example 5/Table 4).

25   **Use of FolK as a target for anti-infective development**

Folate is an essential cofactor in many important metabolic processes in

bacteria, such as purine, pyrimidine, amino acid and pantothenate biosynthesis.

Unlike mammalian cells, bacteria are unable to utilize exogenous folate derivatives,

and therefore must synthesize folate de novo. Bacterial folate biosynthesis occurs via

30   two converging pathways, the non-essential para-amino-benzoate (pABA) synthesis

pathway, and synthesis of the pterin precursor, to which pABA is subsequently

attached to form the folate precursor. Enzymes that catalyze steps in the folate

biosynthesis pathway are essential and well conserved across all bacterial species,

and those that act in early steps such as FolK have no direct homologs in mammals.

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Thus FolK is an attractive target for the development of broad-spectrum antibacterial agents.

Assays for measuring FolK activity

FolK (HPPK) 7,8-dihydroxymethylpterin-pyrophosphokinase activity is monitored individually or in conjunction with downstream enzyme in folic acid biosynthesis pathway.

FolK activity is monitored directly by HPLC assay. FolK substrate (7,8-dihydro-6-hydroxymethylpterin) is commercially available from Schircks Laboratories (Swizerland). FolK is preincubated in reaction buffer containing 50 mM Tris-HCl (pH 8.0), 50 mM KCl, 20 mM $MgCl_2$, 5 mM ATP, 0.1 mg/ml BSA, 2.5 mM dithiothrietol. Reaction is started by addition of stock solution of 7,8-dihydro-6-hydroxymethylpterin in DMSO (100 µM final concentration). Reaction is terminated by addition of equal volume of 8M Guanidinium hydrochloride and applied directly on HPLC. Starting material and reaction products are efficiently separated on ODS (C18) column. Reaction components are detected and quantified by analysis of UV absorbance at 254 nm.

FolK activity is monitored by end-point assay coupled with excess of Sul enzyme. Activity is calculated from quantification of the radioactivity incorporated in final product (7,8-dihydropteroate).

EXAMPLE 20
ALLOIOCOCCUS OTITIDIS ENCODED FOLP (SUL)- DIHYDROPTEROATE SYNTHASE (DHPS)

The *Alloiococcus otitidis* ORF-1811 (Seq. ID No. 53) encodes a homolog of *B. subtilis* dihydropteroate synthase that catalyzes the condensation of pABA (para-aminobenzoic acid) with 6-hydroxymethyl-7,8-dihydropterin pyrophosphate, one of the early steps in bacterial folate biosynthesis. The polypeptide encoded by this ORF is set forth in Seq. ID No. 54. (see Example 5/Table 4)

FOLP AS A TARGET FOR ANTI-INFECTIVE DEVELOPMENT

Folate is an essential cofactor in many important metabolic processes in bacteria, such as purine, pyrimidine, amino acid and pantothenate biosynthesis. Unlike

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mammalian cells, bacteria are unable to utilize exogenous folate derivatives, and therefore must synthesize folate *de novo*. Bacterial folate biosynthesis occurs via two converging pathways, the non-essential para-amino-benzoate (*p*ABA) synthesis pathway, and synthesis of the pterin precursor, to which *p*ABA is subsequently

5   attached to form the folate precursor. Enzymes that catalyze steps in the folate biosynthesis pathway are essential and well conserved across all bacterial species, and those that act in early steps such as FolP (Sul) have no direct homologs in mammals. In fact, dihydropteroate synthase (FolP or Sul) is the target for known antibiotics sulfonamides which are competitive inhibitors of FolP/Sul as *p*ABA

10   analogues. Thus FolP (Sul) still remains an attractive target for development of broad-spectrum antibacterial agents.

Suitable assays for measuring FolP/Sul activity

        Sul (DHPS) 6-hydroxymethy-7,8-dihydroneopteroate synthase activity is

15   monitored individually or in conjunction with upstream enzymes in folic acid biosynthesis pathway (FolB and/or FolK).

        DHPS activity is monitored directly by counting the amount of radioactivity incorporated in 6-hydroxymethy-7,8-dihydroneopteroate when using radioactively labeled *p*-aminobenzoic acid (*p*ABA). Final product is separated from unreacted

20   *p*ABA by thinlayer chromatography, paper chromatography or on HPLC equipped with radioactivity detector. DHPS substrate (6-hydroxymethyl-7,8-dihydropterin pyrophosphate) is not commercially available, but is quantitatively synthesized in one step from its oxidized precursor available from Schircks Laboratories (Swizerland). DHPS (20 ng) is added in reaction buffer containing 50 mM Tris-HCl, pH 8.0, 20 mM

25    $MgCl_2$, 0.1 mg/ml BSA, 5 mM dithiothreitol and 0.5 – 10 µM PABA. Reaction is started by addition of stock solution of substrate (6-hydroxymethyl-7, 8-dihydropterin pyrophosphate, 0.05 - 1 µM final concentration). Reaction is terminated by acidification of reaction volume with addition of equal volume of citrate/phosphate or ammonium acetate/acetate buffer, pH 4 containing excess of unlabelled *p*ABA.

30   Quenched reaction is separated by chromatography and the amount of formed product calculated.

        DHPS activity is determined in coupled assay with excess of FolB and FolK enzymes. The advantage of coupled assay is that it makes it possible to use

commercially available FolB (7,8-dihydro-D-neopterin), or FolK (6-hydroxymethyl-7,8-dihydropterin) substrates, thus forming DHPS substrate *in situ*.

EXAMPLE 21

5   ## *ALLOIOCOCCUS OTITIDIS* ENCODED FILAMENTATION TEMPERATURE SENSITIVE GENE A
(FTsA)

The *Alloiococcus* otitidis ORF-2489 (Seq. ID No. 85) encodes a homolog of *E.*

10   *faecalis* FtsA, one of the essential components of bacterial cell division. The *"fts"*
stands for filamentation temperature sensitive and has been assigned to most
bacterial cell division genes due to the fact that these genes were generally
discovered by the isolation of conditional mutants that form filaments at
nonpermissive temperature . The *ftsA* allele was first isolated and identified in *E. coli*

15   by Ricard and Hirota in 1973, and mapped along with *ftsZ* in 1980.The protein
encoded by this ORF is set forth in Seq. ID No. 86. (see Example 5/Table 4).

Bacterial cell division requires formation of a septum at mid-cell that begins
with the polymerization of FtsZ into a ring structure at the nascent division site. FtsZ,
another key component of bacterial septation is the first known protein to localize to

20   the division site. In *E. coli*, shortly after the formation of the FtsZ ring, FtsA and ZipA
(another key division component present only in gram-negative bacteria) [7] are
independently recruited to the septal ring, most likely through their direct interaction
with FtsZ. Subsequent assembly of other division components at the septum requires
FtsA as well as FtsZ.

25

FtsA as a target for anti-infective development

Like FtsZ, FtsA homologs are present and highly conserved in almost all
eubacteria. FtsA is essential for cell division and its deletion leads to impaired cell
division and sporulation defect. In addition, *E. coli* cells have to maintain critical ratio

30   of FtsA to FtsZ in order for proper cell division to occur. FtsA belongs to the
actin/DnaK/sugar kinase family of proteins. In *B. subtilis,* FtsA acting as a dimer not
only binds ATP but also hydrolyzes ATP. As briefly stated above, *in vivo* and *in vitro*
evidence have demonstrated that FtsA and FtsZ from various bacterial species

directly interact. Taken all together, targeting at FtsA especially at its interaction with FtsZ might lead to identification of broad-spectrum antibacterial agents.

Assays for measuring FtsA activity

5

ATPase activity of FtsA is assayed by following the formation of ^{32}Pi from [γ-^{32}P]-ATP. The reaction mixture containing 50 mM Tris-HCl (pH7.2), 50 mM potassium acetate, 1 mM DTT, 10 mM MgCl$_2$ and different concentrations of [γ-^{32}P]-ATP is incubated for 5 minutes at 37°C. The reaction is started by addition of 50 nM purified

10   FtsA of *Alloiococcus*. The reaction is stopped with 1.5% ammonium molybdate in 0.5N sulfuric acid, and the radioactive Pi extracted into isoamyl alcohol and counted.

Interaction between FtsA and FtsZ is detected quantitatively using yeast two-hybrid system as described. Briefly, *Alloiococcus ftsZ* is cloned into yeast two-hybrid bait vector pLexA (Clontech) to generate a LexA-FtsZ fusion with DNA-binding

15   property. *Alloiococcus ftsA* is cloned into the target vector pB42AD (Clontech) to fuse FtsA to the activating domain. Both plasmids are then transformed into a *Saccharomycyces cerevisiae* strain containing a *lacZ* reporter under the control of multiple LexA operators. β-Galactosidase activity is determined to quantify relative strength of FtsA-FtsZ interaction.

20

EXAMPLE 21

ALLOIOCOCCUS OTITIDIS ENCODED FILAMENTATION TEMPERATURE SENSITIVE GENE Z (FTSZ)

25   FtsZ is an essential protein that forms a cytokinetic ring (Z-ring) that drives cell division in bacteria. FtsZ has been identified in most prokaryotic species with the exception of *Chlamidia*, a *Ureaplasma* species and *Crenarchaea*. FtsZ and Z-ring formation are most extensively studied in *E. coli*. FtsZ is an abundant cytoplasmic protein which is present at ~ 10^4 copies per cell, and is the first protein to be localized

30   to the division site. Z-ring is required throughout septation and directs the ingrowth of septum in part by recruiting other cell division protein to the division site. Another function is suggested by FtsZ homology to eukaryotic tubulins. Like tubulin, FtsZ is a GTPase and undergoes GTP/GDP-dependent polymerization. Recent studies showed that Z-ring is a very dynamic structure suggesting that GTP-dependent

assembly/disassembly of Z-ring might provide constriction force to power cell
division. Homologue of this gene identified in *Alloiococcus otitidis* is described in
Example 5/Table 4 (Seq. ID No 83). The protein encoded by the gene is set forth in
Seq. ID No. 84.

5

GTPase activity

FtsZ is a GTPase that contains the tubulin-signature nucleotide-binding motif
GGGTGS/TG. Like in □□□-tubulin dimer, the active site for GTP-hydrolysis appears
to be shared between two subunits where the GTP-binding pocket is provided by one
10 subunit while the GTPase-activating T7 loop comes from the other subunit. This view
is supported by genetic analysis as various mutations that inhibit FtsZ GTPase
activity map in the T7-loop region and a conserved Asp-residue in T7-loop is found to
be involved in the coordination of the cation involved in GTP hydrolysis. FtsZ
GTPase activity is Mg^{2+}-dependent and is stimulated by KCl.

15

Polymerization

In vivo, about 75% of FtsZ is present as multimers. *In vitro*, FtsZ forms a
variety of structures at various conditions. FtsZ assembles into thin protofilaments
with GTP and formation of FtsZ polymers is coupled to GTP hydrolysis: when GTP
20 runs out, polymers disassemble. Protofilaments assemble into sheets and bundles in
the presence of multimolar amounts of either Mg^{2+} or Ca^{2+} or by addition of DEAE-
dextran. In addition, ZipA protein induces bundling of FtsZ polymers. With GDP, FtsZ
assembles into curved filaments and minirings.

25 ## Interactions with other proteins

In *E. coli*, at least nine different proteins are localized to the division septum and
are required for cell division to proceed. Among them two proteins, ZipA and FtsA,
are shown to interact directly with FtsZ. Both of these proteins localize to the division
site independently from each other, but require FtsZ for localization. ZipA is an
30 integral membrane protein which is thought to mediate invagination of cell membrane
by linking the membrane to constricting Z-ring. Interaction between ZipA and FtsZ is
confined to C-terminal portion of ZipA (residues 185-328) and conserved 17-amino
acid region on C-terminus of FtsZ. FtsA is an actin-like membrane-associated protein

which possesses ATPase activity and might provide energy required for Z-ring dynamics. Interaction between FtsZ and FtsA is not studied in great detail, it is shown that C-terminus of FtsZ is required. The remaining division proteins require both ZipA and FtsA for their localization to Z-ring.

5

FtsZ as a target for anti-infective development

FtsZ is an essential protein for cell division/bacterial viability. Knock-out *ftsZ* mutants fail to divide and, as a result, filament and die. The target is widely

10   conserved throughout bacterial kingdom implying that FtsZ-specific inhibitor would have a broad-spectrum antibacterial activity. The potential drawbacks of the target might include the presence and the essential role of a homolog (tubulin) in eukaryotes and an intrinsic difficulty in inhibiting protein-protein interactions by small molecules. Although this target is being studied extensively, no FtsZ-specific

15   compounds are reported up to date.

Assays for measuring FtsZ function

Polymerization of FtsZ is measured by light scattering assay as described previously. FtsZ (12.5 μM) is incubated in 200 μl of polymerization buffer (50 mM

20   MES/NaOH, pH 6.5, 50 mM KCl, 5 mM $MgCl_2$, 10 mM $CaCl_2$) in a fluorescence cuvette with a 1 cm path length. The sample is maintained at 30°C, polymerization is induced by addition of 20-500 μM GTP. Light scattering is measured at 90°, both excitation and emission wavelengths are set to 350 nm, slit width is 2 nm. Alternatively, the amount of polymerized FtsZ is analyzed by sedimentation and

25   subsequent quantification of precipitated FtsZ by SDS-PAGE, Coomassie staining and densitometric scanning. In addition, polymers are observed by electron microscopy. This assay represents either primary or secondary/confirmatory assay.

GTP binding of FtsZ is monitored by the covalent cross-linking of [γ-^{32}P]GTP (3000 Ci/mmol) to FtsZ in a previously described competition assay. FtsZ (3 μg) is

30   incubated in 20 μl of 50 mM MES/NaOH, pH 6.5, 100 mM KCl, 4 mM $MgCl_2$, 1 mM EDTA, 0.1 mM EGTA and 0.5 mM DTT. Various amounts of non-labeled competing nucleotide (GTP or GTP analogs) and 0.1 mM [γ-^{32}P]GTP are added, samples are incubated at 0°C for 15 min, then UV cross-linked for 5 min and analyzed by SDS-

PAGE on 12% gel, autoradiography and densitometric scanning. This assay represents a secondary/confirmatory assay.

The GTP hydrolytic activity of FtsZ is monitored by thin-layer chromatography (TLC) as described previously. Briefly, the reaction mixture consists of 5 mM of [γ-
5   ^{32}P]GTP (40 mCi/mmol), 15 mM magnesium acetate and 0.25-2 mg/ml of FtsZ in reaction buffer (40 mM Tris-acetate, pH7, 200 mM potassium acetate, 2 mM EDTA, 1 mM DTT and 0.5% Triton X-100), aliquots are separated by TLC and amount of GTP converted to GDP is determined by spot-densitometry. Alternatively, GTPase activity is measured either by quantitation of the non-radioactive inorganic phosphate with
10 the malachite green-molybdate reagent as described previously or by quantitation by scintillation counting of radioactive inorganic phosphate released after hydrolysis of [γ-^{32}P]GTP (26). This assay represents either primary or secondary/confirmatory assay.

Among interactions of FtsZ with various cell division proteins, interaction
15 between FtsZ and ZipA is characterized the best. ZipA –induced bundling of FtsZ is measured by the light scattering assay that is described above, both proteins are used at ≥5 μM.

EXAMPLE 22

20 ### ALLOIOCOCCUS OTITIDIS ENCODED GYRA/GYRB (DNA GYRASE, TOPOISOMERASE II) AND GRLA/GRLB (TOPOISOMERASE IV)

DNA topoisomerases: topoisomerases modulate the topological state of DNA in cells. This involves binding to DNA, introducing single or double stranded breaks
25 in the DNA, passing DNA molecules through the break and rejoining the break. This controls the levels of positive and negative supercoiling of DNA and functions in catenation/decatenation. Controlling the topological state of DNA is critical to the fundamental processes of transcription, recombination, replication and partitioning of the chromosome. There are two main categories of topoisomerases, type I and type
30 II. Type I topoisomerases introduce single stranded breaks in DNA whereas type II enzymes introduce double stranded breaks. GyrA/GyrB (gyrase) and GrlA/GrlB (topoisomerase IV) are both type II enzymes that are essential for cell viability.

DNA gyrase (GyrA/GyrB) is a type II topoisomerase that functions to control the degree of supercoiling in double stranded DNA. It is essential for viability and

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plays central roles in replication, repair, recombination and transcription of DNA. Gyrases have the ability to introduce double stranded breaks in DNA molecules while remaining bound to the DNA through phosphotyrosine bonds, pass uncut DNA through the break and then rejoin the breaks, with repeated cycles being driven by

5   the hydrolysis of ATP. Gyrase has the unique ability to introduce negative supercoils in closed circular DNA and also functions to catenate/decatenate DNA duplexes. The generation of negative supercoiling is important for initial stages in replication. DNA gyrase from *Escherichia coli* has been studied in detail. It is a complex of two subunits of GyrA (encoded by *gyrA*) and two subunits of GyrB (encoded by *gyrB*) (ie.

10   A_2B_2 complex). The subunits are organized in discreet domains. An N-terminal domain of GyrB harbors ATPase activity while the C-terminal domain is thought to interact with the GyrA subunit, and is involved in DNA binding. The N-terminal domain of GyrA is apparently involved in DNA strand breakage-ligation reactions while the C-terminal segment is involved in DNA binding. Crystal structures of the

15   DNA strand breakage/reunion domain of *E. coli* GyrA, and the N-terminal ATPase domain of *E. coli* GyrB have been determined. DNA gyrase has also been purified and characterized from gram positive organisms such as *S. aureus*. Comparison of DNA gyrases from several bacteria reveal a high degree of conservation of important domains.

20   Topoisomerase IV (GrlA/GrlB) is a type II topoisomerase but unlike gyrase it does not possess negative supercoiling activity. Its primary role in replication appears to be in the decatenation of multiply linked daughter chromosomes, important for terminal stages of the replication process. Topoisomerase IV has been purified and characterized from gram negatives eg. *E. coli*, (where the GrlA/GrlB

25   subunit homologs are designated ParC and ParE), and gram positives eg *S. aureus*. Homologs of thse gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID Nos 17 and 19). The proteins encoded by the genes are set forth in Seq. ID Nos. 18 and 20.

GyrA/GyrB (Gyrase) and GrlA/GrlB (topoisomerase IV) as targets for anti-infective development:

Alloiococcus otitidis is an infectious organism associated with disease, and

5   consequently, novel antimicrobials to combat these infections are desirable. DNA

gyrase and Topoisomerase IV is essential for bacterial viability and is a well-

established and validated antibacterial target.

Purification of DNA gyrase and topoisomerase IV from *Alloiococcus*
10   ***otitidis***

Genes encoding the GyrA/GyrB and GrlA/GrlB subunits or their functional

domains are obtained using polymerase chain reaction amplification of the genomic

region encoding them. The genes are then subcloned into standard expression

vectors, with or without affinity tags. The enzyme is then overexpressed in

15   *Escherichia coli* and purified using a standard tag system or conventional

chromatography.

Measurement of gyrase and topoisomerase IV by kinetoplast DNA decatenation assay:

20   Type II topoisomerases introduce double stranded breaks in DNA and

mediate catenation/decatenation of DNA. Topoisomerase IV activity is readily

determined with decatenation assays using as substrate kinetoplast DNA (KDNA)

from *Crithidia fasciculata*. The DNA isolated in this procedure is a highly networked

series of catenated double stranded minicircles and is easily be pelleted by

25   centrifugation. The activity of topoisomerase II enzymes results in the release of

decatenated DNA minicircles from the networked KDNA. These have a high mobility

in agarose gels and migrate into the gel ahead of the networked material, which has

very low mobility, allowing for determination of decatenation activity using ethidium

bromide stained agarose gel electrophoresis.

30   Alternatively, using radiolabeled KDNA, the level of decatenation activity is

measured by counting radioactivity remaining in reaction supernatants following

centrifugation to pellet the networked material. Typical conditions used for assaying

decatenation activity of *S. aureus* and *E. coli* topoisomerase IV activity are as follows:

C. fasciculata KDNA (0.9 mg/ml) is incubated in 40 μl of reaction buffer (50 mM Tris-

35   HCl, pH 7.7, 5 mM MgCl$_2$, 5 mM DTT, 50 μg/ml bovine serum albumin, 1.5 mM ATP

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and 350 mM potassium glutamate) with appropriate amounts of the Grl subunits, for
1 hour at 37°C. If non radiolabeled KDNA is used, these reactions can be stopped
and analyzed by agarose gel electrophoresis, or for radioassays, the reaction is
stopped by gentle mixing with 10 μl of stop solution (50 % glycerol, 50 mM EDTA (pH
8.0), 2.5 % SDS and 0.1 % bromphenyl blue) and centrifuged at 15 000 x g for 5 min
at 20° C. Decatenation activity is determined by counting radioactivity in 25 μl of the
supernatant in a scintillation counter. Alternatively, a modified assay employing flow
injection fluorometry of 4', 6-diaminidino-2-phenylindole (DAPI) treated supernatants
has been described that could be suitable for moderate throughput non radioactive
assays, or filtration of the reactions through appropriate filters may efficiently
separate the decatenated species from KDNA. Although the above described
assays were used for topoisomerase IV, modified decatenation reactions using
KDNA isolated from *Leishmania donovani* reveal significant decatenation activity by
gyrase from *E. coli* and *Mycobacterium smegmatis*, indicating the applicability of the
assay to prokaryotic gyrases.

DNA Supercoiling/relaxation assays.

DNA gyrase function is directly assayed using a simple supercoiling assay
typified by that described for the measurement of *Escherichia coli* DNA gyrase
activity. Briefly, incubation of relaxed closed circular plasmid DNA (pUC18, 7.5 nM)
in the presence of DNA gyrase (approximately 10 nM) in 40 mM Tris-HCl (pH 8.0)
buffer containing 25 mM KCl, 4 mM MgCl2, 2.5 mM spermidine and 1.4 mM ATP
buffer results in the introduction of supercoils in the plasmid DNA. Changes in DNA
supercoiling status are readily observed by the alteration of mobility of the DNA in
agarose gels stained with ethidium bromide and comparison to the mobility of relaxed
and supercoiled plasmid template. This strategy is employed for screening for DNA
gyrase inhibitors.

Topoisomerase IV activity is assayed by measuring relaxation of supercoiled
plasmid DNA. A typical relaxation assay used for *S. aureus* topoisomerase IV
activity is as follows: topoisomerase IV enzyme and supercoiled plasmid DNA
(pBR322, 0.6 μg) is incubated in 40 μl 50 mM Tris-HCl, pH 7.7, containing 5 mM
MgCl2, 5 mM DTT, 50 μg/ml bovine serum albumin, 1.5 mM ATP, 5 mM spermidine
and 20 mM KCl, for 30 min at 37°C. Changes in DNA supercoiling status can be

readily observed by the alteration of mobility of the DNA in agarose gels stained with ethidium bromide and comparison to the mobility of relaxed and supercoiled plasmid template

The ATPase activity of topoisomerases is measured using a coupled spectrophotometric ATPase assay described for the GyrB subunit of E. coli. ATPase activity is assayed in 300 µl of 40 mM Tris-HCl (pH 8.0), containing 25 mM KCl, 2.5 mM spermidine, 4 mM MgCl2, 400 µM phosphoenolpyruvate, 250 µM NADH, 3 µl of pyruvate kinase /lactate dehydrogenase mix and ATP (0.5 – 3.5 mM). The reaction is started by the addition of truncated N-terminal derivatives of the GyrB protein (5 µM) containing the ATPase domain. ATPase activity is reflected as a decrease in absorbance of light at 340 nanometer wavelength.

DNA cleavage assay.

Quinolone drugs interfere with the DNA strand breakage-ligation cycle activity of many topoisomerases. Incubation of topoisomerase and linear or supercoiled pBR322 plasmid DNA, or small linear DNA fragments, in the presence of quinolones and magnesium results in the trapping of a complex of topoisomerase, DNA with a double stranded break and the drug. The topoisomerase remains bound to the cleaved DNA, however treatment with a denaturant such as SDS or proteinases remove/degrade the gyrase, releasing the cut DNA. Certain consensus sequences representing preferred cut sites of E. coli gyrase in plasmid pBR322 have been identified in template DNA molecules used in these assays. This assay is useful for mode of action studies of inhibitors of gyrase/topoisomerase IV activity and in particular of the strand breakage-ligation function. Cleavage reactions are performed with linear or supercoiled DNA. A typical cleavage reaction using linear DNA to measure cleavage by *E. coli* and *S. aureus* gyrase and topoisomerase IV in the presence of drugs is as follows: gyrase/ topoisomerase IV is incubated in 20 µl 25 mM Tris-HCl (pH 7.5) containing 0.5 mM EDTA, 0.5 mM DTT, 3 µg bovine serum albumin per ml, 10 mM MgCl2, 120 mM KCL, 10 mM ATP, 10 000 dpm of 3' end labeled linear pBR322 plasmid DNA and drug for 1 hour at 37°C. (Note: for *S. aureus*, KCl is replaced with 0.7 M potassium glutamate). Reactions are terminated by adding 5 µl 2.5% SDS-2.5 mg proteinase K per ml and incubating at 37°C for 30 minute, then adding 5 µl 30% glycerol-1% SDS-50 mM EDTA-0.05 % bromophenol

blue. Cleavage products are resolved on 1% agarose gels and visualized by autoradiography.

Additional cleavage assays are also used that measure 1) the linearization of supercoiled plasmid DNA (pBR322), with linearization measured using scanning

5   densitometry of DNA species separated on 1 % agarose gels, or 2) the cleavage of small linear DNA molecules of approximately 100 bp encompassing the preferred cleavage sequence 5'- GGCTGGATGGCCTTCCCCAT – 3' from position 990 in plasmid pBR322. In the latter case, the fragment is produced by PCR and radiolabeled with γ-^{32}P ATP at the 5' end of the top strand. This DNA is incubated

10 with 1.3 pmol DNA gyrase in a total volume of 10 μl 35 mM Tris-HCl (pH 8.0), 24 mM KCl, 2 mM spermidine, 4 mM MgCl2 and inhibitor compound at 37°C for 10 min. Reactions are stopped by addition of 8 mM EDTA and 1% SDS, then treated with 500 μg/ml proteinase K for 2 hours at 37°C. The DNA is then cleaned by phenol-chloroform extraction and ethanol precipitation, resuspended in TE buffer (pH 8.0),

15 and loaded and resolved on 12 % sequencing gels containing 7M urea. In the presence of inhibitors of the strand breakage–ligation function, radioactive cleavage products are detectable by autoradiography. Modifications of this assay whereby one strand of the DNA substrate is labeled with an affinity tag such as biotin and the other is radiolabeled or fluorescently labeled should facilitate rapid separation and

20 detection of cleavage products using streptavidin coated columns or plates, resulting in higher assay throughput.

GYRASE ACTIVITY ASSAYS: DNA REPLICATION:

Early work by Fuller and Kornberg revealed that a partially purified crude

25 soluble fraction derived from *Escherichia coli* cells (designated fraction II) contained the components necessary for replication of plasmids containing oriC (*E. coli* chromosomal origin of replication). Replication mediated by this fraction specifically required supercoiled plasmids. Although the exact makeup of the protein complex mediating the replication was not known, the replication reaction was inhibited by 1)

30 rifampicin, and 2) nalidixic acid and novobiocin, indicating essential roles for both RNA polymerase and DNA gyrase, respectively. Subsequently the reaction was reproduced using replication machinery reconstituted from purified protein HU, DnaA,

DnaC, DnaB, single stranded binding protein (SSB), primase, DNA polymerase holoenzyme, RNA polymerase holoenzyme and GyrA/GyrB.

The requirement for gyrase activity for replication is exploited for the identification of gyrase inhibitors using a replication-based high throughput screen. Gyrase specific inhibitors are identified from the overall pool of replication inhibitors using the secondary assays detailed below. Screening for inhibitors of gyrase in a setting where gyrase is participating in an overall reaction that is essential in bacteria might better select physiologically relevant inhibitors

An assay suitable for high throughput screening of inhibitors of replication (including gyrase and DnaA inhibitors) is based on the replication reaction of Kaguna and Kornberg. This reaction was set up as follows; standard reaction in 25 μl: 40 mM Hepes (pH 7.6), 2 mM ATP, 0.5 mM GTP, CTP and UTP, 50 μg/ml bovine serum albumin, 6 mM phospho creatine, 100μM dATP, dGTP, dCTP and dTTP, γ-^{33}P dTTP (50-150 cpm/pmol total nucleotides) 11mM magnesium acetate,100 μg/mL creatine kinase,85 ng SSB, 48 ng DnaB, 40 ng DnaC, 20 ng primase, 160 ng DNA polymerase III holoenzyme, 800 ng RNA polymerase, 150 ng GyrA, 350 ng GyrB, 120 ng DnaA, 2.5 units topoisomerase I, 190 ng HU, 0.15 ng Rnase H 200 ng supercoiled plasmid template. The reaction is assembled at 0 °C and initiated by incubation at 30°C. Replication reactions are terminated by the addition of EDTA to 20 mM. Incorporation of nucleotides into DNA is measured by filtration through 96 well DEAE filter plates and counting retained radioactivity.

Compounds inhibiting gyrase activity in Alloiococcus otitidis are found as part of a larger program directed at replication. This reaction described above uses the replication machinery of a gram-negative organism, which differs somewhat from the replication machinery of gram positives such as *Staphylococcus aureus* with respect to the specific protein subunits involved. Therefore a similar system specific to *Alloiococcus otitidis* is assembled from the relevant proteins purified from *Alloiococcus otitidis*. Several techniques are then utilized to determine the interaction of inhibitors with Gyr A and GyrB. These are described in the literature and include a) Nuclear magnetic resonance; and b) Capillary electrophoresis.

Example 23

ALLOIOCOCCUS OTITIDIS ENCODED CELL WALL BIOSYNTHETIC ENZYMES MURA

     Bacterial cell wall peptidoglycan (murein) is a large macromolecule of periodic

5   structure whose basic unit, a disaccharide-peptapeptide, is polymerized linearly via

the disaccharide motif and cross-linked laterally via the peptide motif. The process of

bacteria cell wall biosynthesis starts from the transferase MurA, which transfers the

addition of an enolpyruvyl moiety to the 3'-hydroxyl-UDP-N-acetyl glycosamine

(UDP-GluNAc). Subsequently, the reductase MurB reduces the enol ether to the

10   lactyl ether, utilize one equiv. of NADPH and a solvent proton to form UDP-N-acetyl

muramic acid (UDP-MurNAc). Next a series of ATP dependent amino acid ligases

(MurC, MurD, MurE and MurF) catalyze the stepwise synthesis of the pentapeptide

side chain using the newly synthesized carboxylate as the first acceptor site. Each

enzyme is responsible for the addition of one more residue except MurF, catalyzes

15   D-ala-D-ala. MurE in gram negative bacteria catalyzes the meso-2, 6-

diaminopimelate (DAP), while in gram positive bacteria MurE catalyzes L-lysine.

     The product of MurF, UDP-NAM pendapeptide is the final product of the

cytoplasm enzymes and is the most important precusor for further peptidoglycan

biosynthesis. UDP-MurNAc pendapeptide is then and catalyzed at the plasma

20   membrane by the membrane bound enzymes such as the translocase MraY and

transferase MurG.

     UDP-N-acetylglucosamine enolpyruvyl transferase (MurA) catalyzes the first

committed step in bacterial cell wall biosynthesis. The enzyme transfers an

enolpyruvyl group from phosphoenolpyruvate (PEP) to UDP-N-acetylglucosamine

25   (UDP-GluNAc) to the 3'-OH of UDP-GlcNAc by an addition-elimination mechanism

that proceeds through a tetrahedral ketal intermediate. MurA product enolpyruvate

UDP-N-acetylglucosamine (EP-UNAG) is a precursor to UDP- N-acetylmuramate

(UDP-MurNAc), an essential building block for the bacterial cell wall. MurA is

conserved across both gram-positive and gram-negative bacterial species: gram-

30   negative bacteria have one copy of the *murA* and gram-positive bacteria have two

copies. *Alloiococcus otitidis murA* was identified as described in Example 5/Table 4

and its genomic structure set forth in Seq. ID No. 101. The amino acid sequence of

the protein encoded by this gene is set out in Seq. Id No. 102.

Alloiococcus otitidis murA as a target for anti-infective development

MurA in E. coli and Streptococcus pneumoniae has been shown to be essential by gene deletion technique. The essentiality of MurA in gram-positive bacteria such as Streptococcus pneumoniae was demonstrated in that its deletion is
5 fetal. No mammalian homolog to MurA has been reported. MurA is specifically inhibited by the natural product antibiotic fosfomycin. Thus the importance of MurA in peptidoglycan biosynthesis makes it an attractive target for the design of novel antibacterial agent.

10 **Assays for measuring MurA function**

Phosphate detection:

MurA activity is detected by quantitating the UDP-GluNAc-dependent Pi from PEP and assayed by Lanzetta's malachite Green-ammonium molybdate assay. Pi is
15 quantitated by measuring the optical density at A660 nm.

Coupled assay with MurB:

A coupled assay in access of MurB, which reduces the MurA product EP-UNAG G to UDP-MurNAc, couples the MurA transferase activity with NADPH
20 oxidation. The oxidation of NADPH is monitored at 340 nm and is stoichometric with the production of EP-UNAG.

Fluorescence experiments

Fluorescence experiments to detect murA are performed using the
25 hydrophobic fluorescence probe 8-anilino-1-naphthalene sulfonate (ANS). The fluorescence quenching of MurA/ANS solutions upon addition of UDP-GlcNAc or pyruvate-P is concentration dependent and in a saturating manner.

Isothermal titration calorimetry

30 The binding of UDP-GluNAc to MurA is studied in the absence and presence of the antibiotic fosfomycin by isothermal titration calorimetry. Fosfomycin binds covalently to MurA in the presence of UDP-GluNAc and also in its absence as

demonstrated by MALDI mass spectrometry. Novel Fosfomycin analogs and other antibiotics that bind to *mur*A are also identifiable using isothermal titration chemistry.

Capillary electrophoresis-based enzyme assay

5   A capillary electrophoresis-based enzyme assay for MurA is described by Dai and colleagues . This method, based on UV detection, provides baseline separation of one of the reaction products, EP-UNAG, from substrates PEP and UDP-GlcNAc within 4 min. The other product, phosphate, is not detectable by UV at 200 nm. Quantitation of individual components, substrates or product, is be accomplished

10   based on the separated peaks. This assay is also used to detect novel antibiotics, which inhibit murA activity.

EXAMPLE 23

ALLOIOCOCCUS OTITIDIS ENCODED CELL WALL BIOSYNTHETIC ENZYMES MURB

15

      MurB, the UDP-*N*-acetyl enolpyruvyl glucosamine reductase, commits the second step of bacterial cell wall biosynthesis in cytoplasm and is responsible for the reduction of the enol ether to the lactyl ether, utilizes one equiv. of NADPH and a solvent proton. The product of MurB is UDP-N-acetylmuramic acid (UDP-MurNAc), the linker of the peptide

20   and glycan portions of cell wall precursor UDP muramyl-pentapeptide. MurB from *E. coli* is a 342 amino acid protein, which has a distinctive yellow color characteristic of bound flavin as its co-factor. The biochemistry characterization and X-ray crystal structure of MurB in *E. coli*, in *Staphylococcus aureus* and *Streptococcus pneumoniae* have been studied extensively. The gene Alloiococcus oitidis murB was identified as disclosed as

25   described in Example 5, and is set out in Seq. ID No. 39. The amino acid sequence of the protein encoded by this gene is set out in Seq. ID No. 40.

Alloiococcus oitidis murB as a target for anti-infective development

30   The essentiality and unique function of MurB in prokaryotic cells and the absence of homologue in eukaryotic cells make it an attractive novel antibacterial target. To date, no small molecule inhibitors of MurB have been reported.

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Alloiococcis oititidis ORF-1263 (*murB*) (Seq. ID No. 39) encodes enzyme UDP-*N*-acetylenolpyruvylglucosamine Reductase (MurB) as shown by sequence homology.

5   **Assays for measuring *Mur*B activity**

     Spectrophotometric assay monitoring NADPH consumption:

MurB activity is typically monitored by its biochemical reaction in which NADPH reduces the bound FAD and resulting decrease in absorbance at 340 nm. Enzyme is maximally activated in the presence of K+, NH^4 at cation concentrations

10   between 10-50 mM.

Coupled assay with *MurC*:

In designing an end point assay for high through put screen (HTS), a novel coupled assay in access of UDP-MurNAc L-alanine synthase (*MurC*) was developed

15   at Wyeth. This assay utilizes the biochemically synthesized *MurA* product EP-UNAG as substrate, coupled with limited *Mur*B and excess *MurC* in the reaction with all other substrates/components involved. In this assay, *Mur*B is responsible for the reduction of the enol ether to the lactyl ether, and the follow up enzyme *MurC* catalyzes the ATP dependent ligation of the first of the five amino acids of UDP-

20   peptapeptide with a release of one molecule of phosphate. After 60 minutes of incubation, color reagent malachite green was added and phosphate was detected spectrophotometrically.

Fluorescence binding assay

25   A fluorescence method developed at Wyeth is used to determine the binding potency (Kd value), stoichiometry and nature of binding site of substrates and inhibitors interactions with *Mur*B enzymes. This assay is based on changes in intrinsic fluorescence of inhibitor and/or enzyme, upon formation of enzyme-inhibitor complex. Oxidized form of *Mur*B consists of two fluorescent groups, namely

30   tryptophan residues and the cofactor FAD. Upon binding inhibitor or substrate, local changes in the solvent environment of these groups or overall conformational and electronic changes occur in the enzyme due to which the fluorescence emission is altered. For instance, inhibitor binding significantly quenched the fluorescence and

altered the solvent environment of FAD to a less polar environment. The changes in the fluorescence of the FAD moiety are used to estimate binding constants for *Mur*B inhibitors. Binding experiments are set up in which a fixed concentration of enzyme is titrated with increasing concentrations of the inhibitor. In typical inhibitor binding

5   experiments, the fluorescence emission of the FAD moiety is quenched due to specific interactions of the inhibitor with *Mur*B enzymes and the binding site was saturated at micromolar concentrations of inhibitor. The changes in the fluorescence are fitted to mathematical binding models to determine binding affinity.

10   **Temperature-jump isothermal denaturation procedure**

Temperature-jump isothermal denaturation procedure with various methods of detection is used to evaluate the quality of putative inhibitors of *Mur*B discovered by high-throughput screening. Three optical methods of detection-ultraviolet hyperchromicity of absorbance, fluorescence of bound dyes, and circular dichroism-

15   as well as differential scanning calorimetry are used to dissect the effects of two chemical compounds and a natural substrate on the enzyme. The kinetics of the denaturation process and binding of the compounds detected by quenching of flavin fluorescence are used to quantitate the dose dependencies of the ligand effects.

20   **NMR studies**

NMR studies are performed using perdeuterated, uniformly 13C/15N-labeled samples of *Mur*B. In the case of substrate-free *Mur*B, one or more backbone atoms are assigned for 334 residues (96%). For NADP+-complexed *Mur*B, one or more backbone atoms are assigned for 313 residues. The strategies used for obtaining

25   resonance assignments are known. Localizing the NADP+ binding site on the MurB enzyme is also studied by NMR methodology.

EXAMPLE 25

ALLOIOCOCCUS OTITIDIS ENCODED CELL WALL BIOSYNTHETIC ENZYME, *MURC*

30

Uridine diphosphate-N-acetylmuramate:L-alanine ligase (MurC) catalyzes the third chemical step of bacterial cell wall biosynthesis. This enzyme is a nonribosomal peptide ligase which utilize ATP to form an amide bond between L-alanine and UDP-

N-acetylmuramic acid (UDP-MurNAc). This ATP-dependent ligation adds the first of five amino acids to the sugar moiety of the peptidoglycan precursor. Also, in this reaction, ATP is converted to ADP with release of one molecule of inorganic phosphate. Thus MurC reaction is an essential step in cell wall biosynthesis for both

5   gram-positive and gram-negative bacteria. The genetic, biochemistry analysis and crystal graphic studies of MurC in gram-negative bacteria *E. coli* have been extensively studied. Characterizations of MurC in other pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* have also been documented.

10   ***Alloiococcis otitidis* encoded MurC as a target for anti-infective development**

The *Alloiococcis otitidis* ORF-2602 (*murC*, Seq. ID No. 95) encodes enzyme UDP-MurNAc:L-alanine ligase (*MurC*) as determined by sequence homology. This enzyme presents a target for the development of novel anti-infectives to treat the

15   disease(s) caused by this pathogen. Novel compounds identified using combinatorial chemistries are assayed for their inhibitory effect on *MurC* activity using one of the asssays set out below.

Assays for measuring MurC activity

20   **Spectrophotometric assay detecting phosphate release:**
MurC activity is detected by the inorganic phosphate production. Typically the reaction mixture contains substrates ATP, L-alanine, UDP-MurNAc, DTT, $MgCl_2$ and MurC enzyme. After 20 minutes incubation, the reaction is quenched with the addition of malachite Green-ammonium molybdate for a colored reaction.

25   Absorbance at 660 nm is read 5 minutes after the quench. Absorbance values are converted to concentration of Pi with standard curves using KH_2PO_4, which is prepared under identical conditions without the enzyme MurC.

Spectrophotometric assay detecting formation of ADP

30   Due to the conversion of ATP to ADP in MurC reaction, the production of ADP is monitored in coupled enzymes spectrophotometrically. In this reaction, in addition to MurC substrate UDP-MurNAc, L-alanine and ATP, NADH, phosphoenolpyruvate, $MgCl_2$ and $(NH_4)_2SO_4$, two other coupled enzymes pyruvate

kinase and lactase dehydrogenase are also presented. Reaction mixtures without
ATP and MurC are incubated at 37°C for 10 min before ATP is added for another
minute. Reaction is then started by the addition of MurC. The decrease of NADH
absorbance at 340 nm is monitored spectrophotometrically. One unit of activity
5   corresponds to 1 umol of ADP formed per hour.

L-Alanine radio-labeled assay:

       The MurC enzyme activity in this assay is measured as endpoint using ^{14}C-L-
alanine and ATP incubated with $MgCl_2$, and $(NH_4)_2SO_4$ in 100 mM Tris/HCl, pH 8.0.
10   Reaction is initiated by the addition of the catalytic amounts of MurC. Samples of the
reaction mixture are then mixed with glacial acetic acid and then stored at 4°C.
Remaining ^{14}C -L-alanine is separated from ^{14}C -UDPMurNAc on SCX columns run
under vacuum. Quenched reaction samples are supplemented with equilibration
buffer and counted using a liquid scintillation counter.

15

EXAMPLE 26

ALLOIOCOCCUS OTITIDIS ENCODED CELL WALL BIOSYNTHETIC ENZYMES MURD

       Bacterial UDP-N-acetylmuramyl-L-alanine:D-glutamate ligase (MurD), a
20   cytoplasmic peptidoglycan biosynthetic enzyme, catalyzes the fourth step of bacterial
cell wall biosynthesis. In this reaction, MurD catalyzes ATP-dependent addition of D-
glutamate to an alanyl residue of the UDP-N-acetylmuramyl-L-alanine (UDP-
MurNAc-L-Ala) precursor, generating the UDP-MurNAc-dipeptide. The formation of a
peptide linkage between the amino function of D-glutamate and the carboxy
25   terminius of UDP-N-acetylmuramuamyl-L-alanine is generated through this reaction.
The stoichiometric consumption of ATP supplies the energy needed for this peptide
bond formation with concomitant generation of ADP and orthophosphate. The murD
genes were cloned and characterized from gram-positive bacteria of Staphylococcus
aureus and Streptococcus pyogenes, and gram-negative bacteria from Escherichia
30   coli, Haemophilus influenzae, Bacillus subtilis. Structures of MurD from E. coli and
MurD complexed with its substrate UDP-MurNAc-L-Ala have been solved to 2.0 A
resolution. The role of specific amino acids at the active site of MurD have been
extensively studied using the ortholog and paralog amino acid invariants. Homologue

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of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 89). The protein encoded by the gene is set forth in Seq. ID.No. 90..

Alloiococcus otitidis encoded MurD as a target for anti-infective development

5

Due to its high specificity and essentiality, MurD is an attractive target for the development of novel antimicrobial agents. *Alloiococcis otitidis* ORF-2494, by sequence homology, has been shown to encode enzyme UDP-N-acetylmuramyl-L-alanine:D-glutamate ligase (MurD) (Seq. ID. No. 89). Inhibition of MurD activity is

10   used to identify novel antimicrobial agents.

Assays for measuring MurD activity

Spectrophotometric assay detecting phosphate release:

15   MurD activity in the presence or absence of a putative inhibitory molecule of MurD is detected by the orthophosphate production in test tube or in 96-well format. Typically the reaction mixture contains substrates ATP, D-glutamine, UDP-MurNAc-L-Ala, DTT, MgCl2 and MurD enzyme. After 20 minutes incubation, the reaction is quenched with the addition of malachite Green-ammonium molybdate for a colored

20   reaction. Absorbance at 660 nm is read 5 minutes after the quench using Molecular Devices SpectraMax 250 plate reader. Absorbance values are converted to concentration of Pi using orthophosphate standards, which are prepared under identical conditions without the enzyme MurD.

25

Spectrophotometric assay for detecting formation of ADP in the presence or absence of a putative inhibitory mollecule of MurD:

Due to the conversion of ATP to ADP in MurD reaction, the production of ADP is monitored with coupled enzymes of pyruvate kinase and lactase

30   dehydrogenase spectrophotometrically. In this reaction, in addition to MurD substrate UDP-MurNAc-L-ala and ATP, MgCl$_2$ and (NH$_4$)$_2$SO$_4$, there is also in significant access of NADH, phosphoenolpyruvate, and two coupled enzymes pyruvate kinase and lactase dehydrogenase. This protocol monitors ADP formation

in the MurD catalyzed reaction, in the presence or absence of a putative inhibitory molecule of MurD, by the decrease of NADH absorbance at 340 nm.

L-Glutamate radio-labeled assay:

5   The MurD enzyme activity in the presence or absence of putative inhibitors of MurD is also measurable using D-^{14}C- glutamate as an endpoint assay. The reaction mixture contains D-^{14}C- glutamate UDP-MurNAc-L-Ala, ATP, MgCl$_2$, (NH$_4$)$_2$SO$_4$ in 100 mM Tris/HCl, pH 8.0. An HPLC assay with online UV and flow scintillation detects the formation of UDP-MurNAc-L-Ala-D-^{14}C Glu and ADP in each reaction.

10

<div align="center">

EXAMPLE 27

ALLOIOCOCCUS OTITIDIS ENCODED CELL WALL BIOSYNTHETIC ENZYME, MURE

</div>

The fifth step in the cytoplasmic peptidoglycan biosynthetic is catalyzed by
15   MurE. In this step, the monomer units in the *Escherichia coli* and *Staphylococcus aureus* cell wall peptidoglycans differ in the nature of the third amino acid in the L-alanyl-gamma-D-glutamyl-X-D-alanyl-D-alanine side chain, where X is meso-diaminopimelic acid or L-lysine, respectively. Therefore, MurE from *E. coli* is the UDP-N-acetylmuramoyl-L-alanyl-D-glutamate: meso-diaminopimelic acid ligase, and
20   MurE from *S. aureus* is the UDP-N-acetylmuramoyl-L-alanyl-D-glutamate: L-lysine ligase. Thus represents the major difference of MurE from other murein enzymes in cytoplasm. The amino acid residues catalyzed by MurE plays a key role in the integrity of sacculus since it is directly involved in the peptide cross-linkage. MurE reaction is also ATP-dependent, which supplies the energy needed for the peptide
25   bond formation with concomitant generation of ADP and orthophosphate.

The essentiality of *MurE* has been well documented in *E. coli*, in *S. aureus*, as well as other pathogens such as *Haemophilis influenzae,Vibrio cholerae* and *Corynebacterium glutamicum*. Gene *murE* has been shown to be essential in bacteria. Homologue of this gene identified in *Alloiococcus otitidis* is described in
30   Example 5/Table 4 (Seq. ID No 25). The protein encoded by the gene is set forth in Seq. ID No. 26.

Alloiococcus otitidis MurE as a target for anti-infective development

<div align="center">-123-</div>

Alloiococcis otitidis ORF-851, by sequence homology encodes enzyme UDP-
N-acetylmuramyl-L-alanine-D-glutamate ligase: meso-diaminopimelic acid/or L-
Lysine (MurE) (Seq. ID No 25). MurE activity in the presence or absence of a

5   putative inhibitory molecule of MurE activity is used to identify novel antimicrobial l
agents, which may be used ti treat disease caused by *Alloiococcis otitidis.*

Assays for measuring MurE activity

Radio labeled substrate assay: meso-A2pm-adding activity

10   Activity of MurE from *Alloiococcis otitidis* in the presence or absence of a
putative inhibitory molecule of MurE activity is measured by using radio-labeled
meso-^{14}C A2pm mixing with ATP, MgCl$_2$, UDP-MurNAc-L-Ala-D-Glu, DTT in 100 mM
Tris/HCl and MurE from *Alloiococcis otitidis* .

15   **Radio labeled substrate assay: L-lysine adding activity**

Activity of MurE from *Alloiococcis otitidis* in the presence or absence of a
putative inhibitory molecule of MurE activity is measured by using radio-labeled UDP-
MurNAc-L-Ala-D-14C-Glu mixing with ATP, MgCl$_2$, DTT, L-lysine in 100 mM Tris/HCl
and MurE from *Alloiococcis otitidis.*

20   In both cases, mixtures are incubated at 37°C for 30 min, and reactions
stopped by the addition of acetic acid. Reaction product is separated by high votage
electrophoresis in 2% formic acid for 45 min. The radio active spots corresponding to
substrate and reaction product are detected by overnight autoradiography, or with
radio scanner.   The spots are also cut out and counted using liquid scintillation

25 . counter.

Example 28

ALLOIOCOCCUS OTITIDIS ENCODED CELL WALL BIOSYNTHETIC ENZYME, MURF

The D-alanyl-D-alanine-adding enzyme MurF encoded by the *murF* gene

30 . catalyzes is the last step of the cytoplasmic peptidoglycan biosynthesis. MurF
performs the ATP-dependent formation of UDP-N-acetylmuramyl-L-gamma-D-Glu-
meso-diaminopimelyl-D-Ala-D-Ala (UDP-MurNAc-pentapeptide). The product of
MurF, UDP-MurNAc pendapeptide, is the final product of the cytoplasm enzymes and

is the most important precusor for further peptidoglycan biosynthesis. UDP-MurNAc pendapeptide is then catalyzed by the plasma membrane bound enzymes such as the translocase MraY and transferase MurG. Homologue of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 3). The protein
5   encoded by the gene is set forth in Seq. ID No. 4.

Alloiococcus otitidis MurF as a target for anti-infective development

Due to its high specificity, essentiality, and importance of its product UDP-MurNAc pentapeptide, MurF is attractive as an antibacterial target. The *Alloiococcis*
10   *otitidis* ORF-48, by sequence homology, encodes enzyme UDP-N-acetylmuramyl-L-alanine-D-glutamate ligase: meso-diaminopimelic acid/or L-Lysine -alanyl-D-alanine-adding enzyme (MurF) (Seq. ID No. 3). MurF activity in the presence or absence of a putative inhibitory molecule of MurF activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by *Alloiococcis otitidis*.

15

Assays for measuring MurF activity

Spectrophotometric assay detecting phosphate release:

Activity of MurF from *Alloiococcis otitidis* in the presence or absence of a
20   putative inhibitory molecule of MurF activity is detected by the inorganic phosphate release in the ATP dependent MurF reaction. This assay detects nonomole amount of Pi in the reaction mixture contains substrates ATP, D-ala-D-ala, UDP-MurNAc-tripeptide, DTT, MgCl$_2$ and MurF enzyme. After 5 minutes incubation, the reaction is quenched with the addition of malachite Green-ammonium molybdate for a colored
25   reaction.

Coupled spectrophotometric assay detecting formation of ADP

Due to the conversion of ATP to ADP in MurF reaction, the production of ADP in the presence or absence of a putative inhibitory molecule of MurF activity, is
30   monitored with coupled enzymes of pyruvate kinase and lactase dehydrogenase spectrophotometrically. In this reaction, the decrease at 340 nm is observed as NADP is consumed in MurF reaction process. The reaction typically contains tris

buffer, substrates ATP, D-ala-D-ala, UDP-MurNAc-tripeptide, DTT, MgCl$_2$, phosphoenopyruvate, NADPH and MurF enzyme.

EXAMPLE 29

5   ### _ALLOIOCOCCUS OTITIDIS_ ENCODED CELL WALL BIOSYNTHETIC ENZYME, MURG

MurG, the last enzyme involved in the intracellular phase of peptidoglycan synthesis, is a membrane-associated glycosyltransferase. MurG catalyzes the transfer of _N_-acetyl glucosamine from UDP to the C4 hydroxyl of a lipid-linked N-
10   acetyl muramic acid derivative (lipid I) to form lipid II. Lipid II is a linked disaccharide that is the minimal subunit of peptidoglycan. Once lipid II is formed, this disaccharide is translocated across the bacterial membrane where it is polymerized and cross-linked to form the peptidoglycan layers. MurG has been shown to be essential for bacterial survival. The inactivation of MurG gene rapidly inhibits peptidoglycan
15   synthesis in exponential growing cells. As a result, various alterations of cell shape are observed, and cell lysis finally occurs. Homologue of this gene identified in _Alloiococcus otitidis_ is described in Example 5/Table 4 (Seq. ID No 87). The protein encoded by the gene is set forth in Seq. ID No. 88.

20   ### _Alloiococcus otitidis_ MurG as a target for anti-infective development

MurG is shown to be associated with the inner face of cytoplasmic membrane, and establishing that the entire peptidoglycan monomer unit assembled before being transferred across the membrane. MurG is a key enzyme at the border
25   line between cytoplasmic and membrane of pepdidoglycan synthesis, thus makes it an attractive target for novel antibacterial agent. Further, no mammalian analogues. of MurG have been identified. Due to its high specificity, essentiality, and importance, MurG is attractive as an antibacterial target.

The _Alloiococcis otitidis_ ORF-2492 has been shown to encode, by sequence
30   homology, glycosyltransferase (MurG) (Seq. ID No......). MurG activity in the presence or absence of a putative inhibitory molecule of MurG activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by _Alloiococcis otitidis_.

Assays for measuring MurG function

Radiolabeled reaction

Activity of MurG from *Alloiococcis otitidis* in the presence or absence of a
putative inhibitory molecule of MurG activity is measured by using ^{14}C labeled *N-*
UDP-GluNAc in the reaction containing UDP-MurNAc-pentapeptide, $MgCl_2$, ATP and
MurG protein. The reaction is stopped after 30 min incubation and by boiling for 3
min. The reaction mixtures are applied to a Whatman I filter paper and subject to
descending chromatography overnight. Radioactivity is located and countered with a
scanner. This assay is also used to identify the specificity of inhibitor of MraY or
MurG, based on the detection of radiolabeled ^{14}C GluNAc incorporated into
membrane precursors.

Fluorometric assay

Based on the decrease in NADPH fluorescence at 465 nm, MurG reaction is
also monitored in a reaction mixture of HEPES buffer, $MgCl_2$, Triton,
phosphoenolpyruvate, and coupled enzymes of lactic dehydrogenase and pyruvate
kinase, UDP-GluNAc and synthesized lipid I analogue in the presence or absence of
putative inhibitors of MurG activity. One micromolar UDP corresponds to 500-
fluorescence unit under the instrument setting.

EXAMPLE 30

ALLOIOCOCCUS OTITIDIS ENCODED *BY HMG CoA REDUCTASE* (MVAA)

Two pathways for isopentenyl diphosphate (IPP) synthesis have been
described in bacteria: the mevalonate pathway and the non-mevalonate (MEP or
GAP-pyruvate) pathway. The mevalonate pathway predominates in the
archaebacteria, gram-positive organisms, yeast and mammals; whereas the MEP
pathway is found in gram-negative organisms, *B. subtilis*, chlamydia, and
mycobacterium. The first HMG CoA reductase gene to be sequenced was cloned
from *P. mevalonii*, in which HMG CoA reductase permits growth on mevalonate as a
sole carbon source. A number of genes of the mevalonate pathway were identified in
S. aureus, S, epidermidis, S. pyogenes, S. pneumoniae, E. faecalis and *E. faecium*.
One of the genes, which encodes for HMG-CoA reductase (*mvaA*), when deleted

severely attenuated for virulence in a mouse model indicating that *mvaA* is essential. Due to its high specificity, essentiality, and importance, *mvaA* is attractive as an antibacterial target. Homologue of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 37). The protein encoded by the gene is

5   set forth in Seq. ID No. 38.

HMG-CoA reductase (MvaA) as a target for anti-infective development

The *Alloiococcis otitidis ORF-* has been shown to encode, by sequence

10   homology, HMG-CoA reductase (*mvaA*) (Seq. ID No 37). MvaA activity in the presence or absence of a putative inhibitory molecule of HMG-CoA reductase (*mvaA*) activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by *Alloiococcus otitidis.*

15   **Assays for measuring HMG-CoA reductase (*mvaA*) activity**

MvaA is purified by standard methods using widely available molecular tags following expression at high level from *E. coli*. Enzymatic activity is monitored in the presence or absence of a putative inhibitory molecule of HMG-CoA reductase activity by following oxidation of NADPH to NADP spectrophotometrically at 340 nm. The

20   assay is carried out in the following buffer: 0.25 mM NADPH, 0.25 mM HMG-CoA, 50 mM NaCl, 1 mM EDTA, 5 mM DTT, 25 mM KH_2PO_4 (pH 7.5). The assay is amenable to HTS in high density screening microtiter plates.

25   **Forward reaction:** Activity of HMG-CoA reductase (*mvaA*) from *Alloiococcus otitidis* in the presence or absence of a putative inhibitory molecule of HMG-CoA reductase activity is measured by reductive deacylation of HMG-CoA to mevalonate as measured the consumption of NADPH to NADP. Unlike other class II HMG Coa reductases, MvaA from *Alloiococcus otitidis*, like *S. aureus,* can use either NADPH or

30   NADH cofactor in the reaction. The following kinetic data describe the reaction: $K_{m(HMG CoA)}$ = 40 µM, $K_{m(NADPH)}$ = 70 µM, $K_{m(NADP)}$ = 100 µM (12). This assay is inhibitable by the statin drug fluvastatin; the K_i was measured at 320 µM, which is four orders of magnitude higher than the K_i for class I HMG-Coa reductases.

Reverse reaction: The oxidative acylation of mevalonate to HMG-CoA in the presence or absence of a putative inhibitory molecule of HMG-CoA reductase activity is also monitored. The following kinetic data describes the reaction: $K_{m(mevalonate)}$ = 670 μM, $K_{m(CoASH)}$ = 390 μM, $K_{m(NADP)}$ = 580 μM (12).

5

EXAMPLE 31

ALLOIOCOCCUS OTITIDIS ENCODED _DIPHOSPHOMEVALONATE DECARBOXYLASE_ (MVAD)

Diphosphomevalonate decarboxylase, encoded by _mvaD_, the final enzyme

10   acting in the mevalonate pathway of IPP synthesis was cloned from _S. aureus_ by Wilding _et al_ in 2000. Insertional inactivation of _mvaD_ could only be accomplished when the strains were supplemented with mevalonate, indicating that _mvaD_ is essential. The final step of the mevalonate pathway leading to IPP is the decarboxylation and dehydration of mevalonate-5-pyrophosphate to form isopentenyl

15   diphosphate by MvaD (diphosphomevalonate decarboxylase).

MvaD homologues are well represented in gram-positive organisms (10). Phylogenetic analysis revealed that the cluster of gram-positive enzymes (39-80% identity) were well separated from the eukaryotic homologues, suggesting utility as an antibacterial target. The _Alloiococcis otitidis_ ORF- 1275b has been shown to

20   encode, by sequence homology, diphosphomevalonate decarboxylase (MvaD) (Seq. ID No. 43). MvaD activity in the presence or absence of a putative inhibitory molecule of diphosphomevalonate decarboxylase (MvaD) activity is used to identify novel antimicrobial agents, which may be used to treat the disease(s) caused by _Alloiococcus otitidis._ The protein encoded by the gene is set forth in Seq. ID No. 44.

25

Example 32

ALLOIOCOCCUS OTITIDIS ENCODED HMG CoA SYNTHASE (MvaS)

5   The second step of the mevalonate pathway leading to IPP is the irreversible
condensation of acetoacetyl-CoA and acetyl-CoA to form HMG-CoA by MvaS (HMG
CoA synthase). It has been shown that mvaS knockout mutant of S. pneumoniae
was attenuated for virulence. Due to its high specificity, essentiality, and importance,
mvaS is attractive as an antibacterial target. Homologue of this gene identified in
Alloiococcus otitidis is described in Example 5/Table 4 (Seq. ID No 35). The protein
10   encoded by the gene is set forth in Seq. ID No. 36.

HMG CoA SYNTHASE (MvaS) AS A TARGET FOR ANTI-INFECTIVE DEVELOPMENT

The Alloiococcis otitidis ORF- has been shown to encode, by sequence
15   homology, MvaS (HMG CoA synthase) (Seq. ID No. 35). MvaS activity in the
presence or absence of a putative inhibitory molecule of HMG-CoA synthase (mvaS)
activity is used to identify novel antimicrobial agents, which may be used to treat
disease caused by Alloiococcus otitidis.

20   **Assays for measuring MvaS function**

MvaS is purified by standard methods using widely available molecular tags
following expression at high level from E. coli. HMG-CoA synthase activity in the
presence or absence of a putative inhibitory molecule of HMG-CoA synthase (mvaS)
is assayed by measuring the loss of the enolate form of acetoacetyl-CoA
25   spectrophotometrically. The reaction is carried out in a buffer containing 50 mM Tris
(pH 9.75), 5.0 mM MgCl$_2$, 500 µM acetyl-CoA, 20 µM acetoacetyl-CoA and enzyme.
The enolate formed is monitored at 302 nm; therefore, as the acetoacetyl-CoA is
consumed the signal is depleted. Using this assay the following kinetic data is
measured: $K_{m(acetyl-CoA)}$ = 350 µM; $K_m^{app}$$_{(acetoacetyl-CoA)}$ = 10 µM. This assay is amenable
30   to HTS in high- high density screening microtiter plates.

Example 33

ALLOIOCOCCUS OTITIDIS ENCODED NICOTINAMIDE ADENINE DINUCLEOTIDE ADENYLYL TRANSFERASE (NADD)

5   Nicotinamide adenine dinucleotide (NAD) is an essential molecule in all living cells. NAD is synthesized via a multi-step _de novo_ pathway or via a pyridine salvage pathway. The enzyme nicotinic acid mononucleotide adenylyl transferase (NaMN AT, EC2.7.7.18) catalyzes the conversion of ATP and nicotinic acid mononucleotide (NaMN) to nicotinic acid adenine dinucleotide (NaAD). The _nadD_ gene, encoding

10   bacterial NaMN AT, is essential for NAD biosynthesis and bacterial cell survival. NadD contains well-conserved the nucleotidyl transferase consensus sequence (GXFXXXHXGH). The adenylyl transferase encoded by the _nadD_ gene prefers NaMN over nicotinomide mononucleotide (NMN) as substrate. Due to its high specificity, essentiality, and importance, _nadD_ is attractive as an antibacterial target.

15   Homologue of this gene identified in _Alloiococcus otitidis_ is described in Example 5/Table 4 (Seq. ID No 91). The protein encoded by the gene is set forth in Seq. ID No. 92.

NICOTINAMIDE ADENINE DINUCLEOTIDE ADENYLYL TRANSFERASE (NADD)
20   AS A TARGET FOR ANTI-INFECTIVE DEVELOPMENT

       The _Alloiococcis otitidis_ ORF- has been shown to encode, by sequence homology, niotinomide adenine dinucleotide adenyl transferase (NadD) (Seq. ID No. 91). NadD activity in the presence or absence of a putative inhibitory molecule of

25   NadD activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by _Alloiococcus otitidis_.

Assays for measuring NadD function
Discontinuous assay

30   NadD activity in _Alloiococcus otitidis_ is measured in the presence or absence of a putative inhibitory molecule of NadD activity. NadD converts nicotinic acid mononucleotide (NaMN) and adenosine triphosphate (ATP) to nicotinic acid dinucleotide (NaAD) and pyrophosphate (PP$_i$). Each PP$_i$ molecule produced by the NadD reaction is then converted to two phosphate

(P_i) molecules in the presence of inorganic pyrophosphatase (PPase). The P_i molecules present are quantitated with a malachite green reagent at 660 nm.

HPLC-based assay: Enzyme activity is measured by HPLC quantitation of the reaction products. A neutralized aliquots from the reaction described

5   above was injected into an HPLC system utilizing a 250 x4.6 mm Supelcosil LC-18 5μm reversed-phase column. The elution conditions: 9 min at 100% buffer A (0.1 M potassium phosphate buffer, pH6.0,6 min at up to 12% buffer B (buffer a, containing 20% methanol, 2.5 min at up to 45% buffer B, 2.5 min at up to 100% buffer B, and hold at 100% buffer B for 5.5 min. The eluate

10   absorbance was monitored at 254 nm.

Continuous assay

In bacteria, NadD combines nicotinic acid mononucleotide (NaMN) and adenosine triphosphate (ATP) to form nicotinic acid adenine dinucleotide (NaAD).

15   NadE then converts NaAD into nicotinamide adenine dinucleotide (NAD) in the presence of ammonia and ATP. In the assay, the NAD product is reduced to NADH

)   with alcohol dehydrogenase (ADH) and ethanol, thus permitting direct spectrometric detection of NADH at 340 nm wavelength. The coupled reaction above also includes inorganic pyrophosphatase (PPase) to prevent accumulation of the pyrophosphate

20   byproduct from the consumption of ATP.

EXAMPLE 34

ALLOIOCOCCUS OTITIDIS ENCODED NICOTINAMIDE ADENINE DINUCLEOTIDE SYNTHASE (NADE)

25
NAD is a central compound in cellular metabolism. The final metabolic step in the pathway is conversion of nicotinamide adenine dinucleotide – product of NadD reaction – to NAD, a step catalyzed by the enzyme NAD synthetase (NadE). NaMN – substrate for NadD – can be formed by three different enzymatic reactions:

30   in the *de novo* pathway from quinolinate, in Preiss-Handler salvage pathway from nicotinic acid, and in the nucleoside salvage pathway by deamindation of nicotinamide mononucleotide. In bacteria, there are no known alternatives for the metabolic steps between NaMN and NAD. Mutants blocked in these steps cannot be recovered as auxotrophs since the required metabolites are not taken up by cells. In

the bacterial cells, the second substrate for NadE is ammonium, as opposed to glutamine for eukaryotes. NadE is an essential and conserved protein in the eubacterial nicotinamide adenine dinucleotide (NAD) biosynthesis pathway. Homologue of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 49). The protein encoded by the gene is set forth in Seq. ID No. 50.

Assays for measuring NadE function:

The *Alloiococcis otitidis ORF-* has been shown to encode, by sequence homology, niotinomide adenine dinucleotide adenyl synthase (NadE) (Seq. ID No. 49). NadE activity in the presence or absence of a putative inhibitory molecule of NadE activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by *Alloiococcus otitidis*.

DISCONTINUOUS ASSAY:

In assay, NadE converts nicotinic acid adenine dinucleotide (NaAD) into nicotinamide adenine dinucleotide (NAD) in the presence of ammonia and ATP. Each PP_i molecule produced by the NadE reaction can then be converted to two phosphate (P_i) molecules in the presence of inorganic pyrophosphatase (PPase). The P_i molecules present can then be quantitated with a malachite green reagent at 660 nm.

HPLC-based assay:

Enzyme activity can be measured by HPLC quantitation of the reaction products. A neutralized aliquots from the reaction described above was injected into an HPLC system utilizing a 250 x4.6 mm Supelcosil LC-18 5μm reversed-phase column. The elution conditions: 9 min at 100% buffer A (0.1 M potassium phosphate buffer, pH6.0,6 min at up to 12% buffer B (buffer a, containing 20% methanol, 2.5 min at up to 45% buffer B, 2.5 min at up to 100% buffer B, and hold at 100% buffer B for 5.5 min. The eluate absorbance was monitored at 254 nm (1).

Continuous assay:

Coupled NadD-NadE assay. NadD and NadE can be detected in one
continuous coupled assay. In first reaction, NadD combines nicotinic acid

5 mononucleotide (NaMN) and adenosine triphosphate (ATP) to form nicotinic acid
adenine dinucleotide (NaAD). NadE then converts NaAD into nicotinamide adenine
dinucleotide (NAD) in the presence of ammonia and ATP. In the assay, the NAD
product is reduced to NADH with alcohol dehydrogenase (ADH) and ethanol, thus
permitting direct spectrometric detection of NADH at 340 nm wavelength. The ·

10 coupled reaction above also includes inorganic pyrophosphatase (PPase) to prevent
accumulation of the pyrophosphate byproduct from the consumption of ATP (this
method can be use as HTS format).

NadE assay. In assay, NadE converts NaAD into nicotinamide adenine
dinucleotide (NAD) in the presence of ammonia and ATP. The NAD product is

15 reduced to NADH with alcohol dehydrogenase (ADH) and ethanol, thus permitting
direct spectrometric detection of NADH at 340 nm wavelength. The reaction above
also includes inorganic pyrophosphatase (PPase) to prevent accumulation of the
pyrophosphate byproduct from the consumption of ATP (this method can be use as
HTS format).

20

EXAMPLE 35

ALLOIOCOCCUS OTITIDIS ENCODED PUTATIVE MEMBRANE PROTEIN *NORA*

An efflux transporter NorA that was originally identified in *Staphylococcus*

25 *aureus* belongs to the family of multidrug resistance (MDR) transporters. NorA is
encoded by chromosomally-located *norA* gene, it has broad substrate specificity and
mediates resistance to various lipophilic and monocationic compounds such as
ethidium bromide (EtBr), cetrimide, benzalkonium chloride, rhodamine 6G,
tetraphenylphosphonium (TPP), chloramphenicol as well as some hygrophilic

30 quinolones such as norfloxacin, ciprofloxacin and oxafloxacin. Increased levels of
norA expression are associated with single nucleotide changes upstream of *norA* in a
putative promoter/operator region and lead to increased pleiotropic resistance. NorA
is a putative membrane protein with 12 predicted membrane-spanning domains and
is classified as a member of major facilitator superfamily (MFS), a subgroup of MDR

transporters characterized by the presence of 12-14 transmembrane segments and the use of proton motive force as an energy source for drug efflux. NorA homologs that belong to MFS family include Bmr and Blt of *Bacillus subtilis*, EmeA of *Enterococcus faecalis* and PmrA of *Streptococcus pneumonia*. The expression of

5   *bmr* gene in *B. subtilis* is upregulated by the product of adjacent *bmR* gene in the presence of inducers (rhodamine 6G and TPP), and there is an evidence that expression of *norA* in *S. aureus* is regulated by AlrS-AlrR two-component regulatory system.

It remains unknown whether the efflux of various toxins is a primary function

10   of NorA. When overexpressed in E. coli, *norA* produces resistance to a broad range of substrates including fluoroquinolones. Everted membrane vesicles prepared from *norA*-expressing *E. coli* exhibit energy-dependent transport of norfloxacin, the transfer is abolished by cyanide m-chlorophenylhydrazone (CCCP) and nigericin but not by valinomycin indicating that NorA-mediated transfer is coupled to the proton

15   gradient of cell membrane. Norfloxacin uptake in everted vesicles as well as NorA-associated resistance phenotype is inhibited by reserpine and verapamil that also inhibit other MDR transporters and are toxic to mammalian cells. Histidine-tagged NorA (NorA-His) was recently overexpressed and purified from *E. coli*, reconstituted into both everted membrane vesicles and proteoliposomes and was shown to

20   function as a self-sufficient efflux pump using fluorescent dye Hoechst 33342. Due to its high specificity, essentiality, and importance, *norA* is attractive as an antibacterial target. Homologue of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 67). The protein encoded by the gene is set forth in Seq. ID No. 68.

25

NorA as a Target for Anti-Infective Development

The *Alloiococcis otitidis ORF*- has been shown to encode, by sequence homology, NorA (Seq. ID No. 67). NorA activity in the presence or absence of a

30   putative inhibitory molecule of NorA activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by *Alloiococcus otitidis*.. Because of broad substrate specificity of NorA, NorA inhibitors should be particularly useful against pathogens that possess multiple drug resistance.

Whole-cell high-throughput screen (HTS) assay that measures NorA activity in the presence or absence of a putative inhibitory molecule of *Alloiococcis otitidis* NorA activity is used to identify potential inhibitors of NorA activity. The assay utilizes *B. subtilis* strain (ΔΔNA) that has both Bmr and Blt genetically inactivated while

5   *Alloiococcis otitidis* NorA is supplied on the plasmid expression vector. The screen is based on the reversing of the resistance of ΔΔNA to EtBr. The exponentially growing cells are inoculated into the wells of a 96-well plate to OD_{600}=0.001, the compounds are added at 20 µg/ml and EtBr is added at 10 µg/ml. Plates are incubated for 18 hrs at 37°C and examined for growth. Compounds that inhibit growth are subsequently

10   tested in the presence/absence of EtBr for toxicity and effectivity. The efflux of EtBr from cells is monitored as described previously. The exponentially growing cells are loaded with EtBr at a concentration of 10 □g/ml for 20 min at 37°C in the presence of reserpine (20 □g/ml). Cells are centrifuged, resuspended to an OD_{600}=0.2 in a minimal medium GM1 alone or in the presence of inhibitor compound. Fluorescence

15   of EtBr is monitored on a fluorimeter at an excitation □ of 530 nm and emission □ of 600 nm..

MONITORING OF HOECHST 33342 EFFLUX

The efflux of fluorescent dye Hoechst 33342 from either everted membrane

20   vesicles prepared from *Alloiococcus otitidis* His-NorA overexpressing *E. coli* or a proteoliposomes reconstituted with *Alloiococcus otitidis* His-NorA is also used to monitor NorA activity in the presence or absence of putative inhibitors of NorA. Everted membrane vesicles are diluted into 2 ml of 50 mM potassium HEPES (pH 7.2), 8.5 mM NaCl, 2 mM magnesium sulfate at a final protein concentration of 40

25   µg/ml. NorA is activated by the addition of either 0.5 mM lactate or 0.1 mM Mg^{2+}-ATP. Hoechst 33342 is used in a range of 12.5 to 200 nM. Inhibitors are added at various concentrations prior to the addition of Hoechst 33342. Fluorescence change is monitored at excitation and emission wavelenghths of 355 and 457 nm respectively in a FluoroMax spectrofluorimeter. For proteoliposome assay, the His-

30   NorA proteoliposomes are diluted into a cuvette containing 2 ml of 20 mM potassium phosphate, 50 mM potassium sulfate, 2 mM magnesium sulfate (pH 7.0) at a protein concentration of 10 µg/ml. The inhibitor compounds and Hoechst 33342 are added at various concentrations and the fluorescence is measured as described previously.

EXAMPLE 36
ALLOIOCOCCUS OTITIDIS ENCODED *OBG GTPASE*

5   The *obg* gene is the second gene in a two-gene operon along with the stage-O sporulation gene *spoOB* in *B. subtilis*. SpoOB is central to the phospho-relay signal cascade that initiates sporulation. Obg is a member of the GTPase superfamily by virtue of homology throughout a small portion of the protein that in other members of the family is responsible for nucleotide (GTP/GDP) binding. Obg

10   is essential for growth. Initiation of sporulation is thought to be triggered by changes in the GTP content of the cell; therefore, the presence of a GTP binding protein in an operon with a central player in the process is suggestive of a role for Obg in sensing GTP levels and transmitting a signal to SpoOB.

It has been shown that Obg is involved in activation of the σ^B transcription

15   factor in *B. subtilis* in response to environmental stress. Cells were depleted of Obg utilizing a construct that put *obg* under the control of an inducible (P_{lac}) promoter. Depletion of IPTG resulted in bacteria that failed to activate σ^B. These studies further showed by yeast-two-hybrid analysis that Obg interacted with several known σ^B regulators, the so-called Rsb proteins.

20   The role Obg plays in transmitting signals important for sporulation and activation of the stress sigma factor may be indicative of the activities that small GTP binding proteins carry out in triggering cell division in response to GTP levels. Due to its high specificity, essentiality, and importance, obg is attractive as an antibacterial target. Homologue of this gene identified in *Alloiococcus otitidis* is described in

25   Example 5/Table 4 (Seq. ID No 71). The protein encoded by the gene is set forth in Seq. ID No. 72.

OBG AS A TARGET FOR ANTI-INFECTIVE DEVELOPMENT

30   Obg is essential for bacterial viability. Conditional lethal alleles revealed that Obg is required for early events in sporulation and is involved in transmitting signals require for activation of the stress sigma factor. The *Alloiococcis otitidis* ORF- has been shown to encode, by sequence homology, obg (Seq. ID No.71). Obg activity in the presence or absence of a putative inhibitory molecule of Obg activity is used to

identify novel antimicrobial agents, which may be used to treat disease caused by *Alloiococcus otitidis*..

Nucleotide binding

5   Obg binding to nucleotide in the presence or absence of putative antimicrobials, which inhibit Obg activity, is monitored by a simple filter-binding assay. *Alloiococcus otitidis* Obg (1-5 µg) is incubated with α^{32}P-GTP (0.2 µCi) in a buffer consisting of 50 mM Tris (pH 8.5), 1.5 mM $MgCl_2$, 0.1 mM EDTA, 200 mM KCl, 10% glycerol for 30 minutes to 3 hours at 37°C. A portion of the reaction mix is

10   spotted on nitrocellulose membrane, washed (50 mM Tris (pH 8.5), 1.5 mM $MgCl_2$, 1 mM DTT) and dried. The membrane is then exposed to X-ray film. Alternatively, the spots are excised and counted. This assay is directly amenable to HTS using filter plates.

GTPase activity

15   The GTP hydrolytic activity of Obg is monitored using thin-layer chromatography (1, 2, 10). Obg and α^{32}P-GTP are incubated in 50 mM Tris (pH 8.5), 1.55 mM $MgCl_2$, 0.1 mM EDTA, 200 mM KCl, 10% glycerol for 30 minutes at 37°C. An aliquot of the reaction is placed on PEI cellulose and the strip developed with 0.5

20   M KH_2PO_4, 1.0 M NaCl (pH 3.7). The spots conforming to GDP and GTP are identified by UV shadowing, excised and counted. .

       Alternatively, the hydrolysis of γ^{32}P-GTP is monitored by assaying for liberated P_i (12). Obg and α^{32}P-GTP are incubated in 50 mM Tris (pH 8.5), 1.5 mM $MgCl_2$, 0.1 mM EDTA, 100 mM KCl, 10% glycerol for 30 minutes to 3 hours at 37°C.

25   The reaction is stopped by the addition of a slurry of charcoal in 1 mM Kpi (pH 7.5), which selectively binds the GTP and GDP. The liberated P_i in the supernatant is monitored by Cerenkov counting. Free P_i is also monitored with the Malachite Green reagent.

Autophosphorylation

30   Obg autophosphorylation is monitored by incubating Obg with γ^{32}P-GTP in 50 mM Tris (pH 8.5), 1.5 mM $MgCl_2$, 0.1 mM EDTA, 100 mM KCl, 10% glycerol for 30

minutes at 37°C. Samples are analyzed following separation on SDS polyacrylamide
gels, drying the gel and exposure to film.

EXAMPLE 37.

5   RPOA, RPOB, RPOC, *AND* RPOD, THE GENES ENCODING THE SUBUNITS COMPRISING
ALLOIOCOCCUS OTITIDIS RNA POLYMERASE: ALPHA, BETA, BETA', AND SIGMA.

RNA polymerase is an enzyme comprised of multiple highly conserved
subunits which catalyzes the DNA template directed polymerization of ribonucleic

10   nucleotides into ribonucleic acid. It is composed of a core enzyme, □2,□,□', along
with a fifth subunit present in stoichiometric amounts, □□□which can catalyze RNA
synthesis non-specifically. Holoenzyme is formed by the introduction of the subunit
□□□, which enhances gene promoter recognition and allows specificity. Homologs of
the genes identified in *Alloiococcus otitidis* are described in Example 5/Table 4 (Seq.

15   ID Nos 7, 9, 11, and 13). The amino acid sequence of the protein encoded by these
genes are set forth in Seq. ID Nos. 8, 10, 12 and 14.

Functions for the individual subunits have been defined biochemically, and
interactions between them have now been deduced structurally by crystallographic
analysis of the enzyme from *Thermatoga thermophila*, and to a lesser extent,

20   *Escherichia coli.* The alpha subunit, encoded by *rpoA*, is required for enzyme
assembly. It also interacts with transcription factors and with DNA elements involved
in enhanced promoter strength. Beta, encoded by *rpoB*, is involved in initiation and
elongation of the polymerization product. Beta' (encoded by *rpoC*), is responsible for
binding of the enzyme to the DNA template. Omega is required to restore denatured

25   RNA polymerase to function *in vitro*. Finally, sigma, encoded by *rpoD*, directs the
enzyme to promoters on the template to enhance specificity of transcription
(polymerization).

ALLOIOCOCCUS OTITIDIS RNA POLYMERASE: ALPHA, BETA, BETA', AND SIGMA AS A
TARGET FOR ANTI-INFECTIVE DEVELOPMENT

Bacterial RNA polymerase is a validated target for antimicrobial

chemotherapy in that several inhibitors have been identified and at least one,

5   rifampin, is in use clinically. Alloiococcus otitidis RNA polymerase holoenzyme is

essential for bacterial viability. The *Alloiococcis otitidis ORFs-* have been shown to

encode, by sequence homology, RNA polymerase holoenzyme (Seq. ID Nos. 7, 9,

11 and 13). Alloiococcus otitidis RNA Polymerase activity in the presence or absence

of a putative inhibitory molecule of Alloiococcus otitidis RNA Polymerase activity is

10   used to identify novel antimicrobial agents, which may be used to treat disease

caused by *Alloiococcus otitidis.*

Assays for the activity of RNA polymerase

Genes encoding the subunits of *Alloiococcus otitidis* RNA polymerase can be

15   obtained using polymerase chain reaction amplification of the genomic region

encoding them. The genes are subcloned into a standard expression vector either

containing an amino acid tag for ease of purification or not. The enzyme are

overexpressed in *Escherichia* coli and purified using a standard tag system or

conventional chromatography .

20   Because RNA polymerase catalyzes the incorporation of single ribonucleotides

into RNA, the incorporation of radiolabelled nucleotides into larger oligonucleotides is

monitored to measure activity of the enzyme in the presence or absence of putative

inhibitors of RNA polymerase activity. An automated high throughput filtration assay

has been previously described for *E. coli* polymerase which uses filterplates

25   containing a hydrophobic membrane and DEAE beads to capture polymerized RNA.

G-less supercoiled DNA is used as a template at 6 ug/ml. Reaction contained 0.5

mM ATP, 0.1 mM UTP, 0.3 mM CTP, approximately 100,000 counts per minute (per

100 ul) [γ-^{33}P] CTP (2000 Ci/mmol, NEN/DuPont), 4 % polyethylene glycol, 4 mM

DTT, 10 mM MgCl$_2$, in 50 mM Tris-acetate (pH 7.8), and 100 mM potassium acetate.

30   The reaction is carried out at 34 degrees C for 40 minutes, with 10% DMSO present

in all reactions. The reaction was stopped by adding 100 ul 15% DEAE-Sephacel

bead slurry in 50% methanol, 20 mM EDTA, and 0.02% NP-40. The reaction was

incubated for 40-60 minutes at room temperature without shaking, and then

transferred to a unifilter plate on a filtermate cell harvester. The wells were washed

six times with 2X PBS and 0.1% NP-40. After washing the bottom of the plate was sealed, and 50 ul scintillation counting liquid was added. Radioactivity was counted using a microplate scintillation counter.

Deconvolution assays are carried out by measuring the inhibition of sigma
5   activity. Because sigma is required only for promoter specificity, polymerization may occur non-specifically if sigma is inhibited. Consequently a second assay is described above that is used to deconvolute activity against sigma.

The binding of putative inhibitory compounds to core enzyme. Several techniques are utilized to determine the interaction of inhibitors with individual
10   subunits and include nuclear magnetic resonance and capillary electrophoresis.

EXAMPLE 38

YPHC, ENCODING A SMALL GTPASE OF UNKNOWN FUNCTION FROM *ALLOIOCOCCUS OTITIDIS*

15

The *yphC* was initially identified in *Bacillus subtilis* in a collaboration between Wyeth and Millennium pharmaceuticals as being essential for growth by insertional mutagenesis. Subsequently it was determined that YphC, the encoded protein, contained two GTPase domains and had some homology to *era*. It was further
20   identified in *Thermatoga maritima* and *Escherichia coli* . While no function has yet been determined for yphC, it appears that the carboxy terminal may contain an RNA binding site. In addition, site directed mutagenesis of four amino acids in the carboxy region were found to be lethal (unpublished results, Millennium). Under non-permissive conditions, strains carrying temperature sensitive alleles of the gene in *E.*
25   *coli* become elongated, and chromosome segregation becomes abberrant, suggesting a role in cell division. Homologue of this gene identified in *Alloiococcus otitidis* is described in Example 5/Table 4 (Seq. ID No 73). The protein encoded by the gene is set forth in Seq. ID No. 74.

YphC from *Alloiococcus otitidis* as a target for antimicrobial chemotherapy

YphC is an essential protein in *Bacillus subtilis* and *E. coli*, and is conserved among bacteria including *Alloiococcus otitidis*. The *Alloiococcis otitidis ORF-* has

5   been shown to encode, by sequence homology, YphC (Seq. ID No. 73). YphC activity in the presence or absence of a putative inhibitory molecule of YphC activity is used to identify novel antimicrobial agents, which may be used to treat disease caused by *Alloiococcus otitidis.*. Consequently it is proposed here that an assay which identified inhibitors of YphC from *Alloiococcus* would result in small molecules

10   which can be developed into effect antimcrobial agents. Additionally, because of the conservation of the enzyme among bacteria, inhibitors of the protein's function from this organism should have broad spectrum activity.

Assays for the GTP hydrolysis by YphC

15   The YphC gene from Alloiococcus otitidis is obtained using polymerase chain reaction amplification of the genomic region encoding it. The gene is subcloned into a standard expression vector either containing an amino acid tag for ease of purification or not. The enzyme is then overexpressed in *Escherichia* coli and purified using a standard tag system or conventional chromatography. Activity of

20   YphC in the presence or absence putative antimicrobial agents is monitored using the assay system described below.

GTP hydrolysis – detection by thin layer chromatography: Reaction is carried out in a 50 ul reaction of 50 mM Tris-Cl (pH 7.5), 400 mM KCl, 5 mM MgCl2,

25   1 mM DTT, 10 uM [a-32P] GTP, and 10 ug purified YphC, at 37 degrees for 10 minutes. The reaction is terminated by transfer of 5 ul samples to 10 ul of ice-cold 20 mM EDTA. Portions are spotted onto polyethyleneimine-cellulose thin layer chromatography plates, which are developed in 0.75 KH2PO4 (pH 3.65). The plate is autoradiographed to identify hydrolysis products.

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        of the autophosphorylation of Era, an essential Escherichia coli GTPase. Mol
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25

WHAT IS CLAIMED IS:

5   1.   A purified or isolated *Alloiococcus otitidis* nucleic acid sequence comprising a
              nucleotide sequence selected from one of odd numbered sequences set forth
              in Seq. ID Nos: 1 to Seq. ID Nos: 105, wherein expression of said nucleic acid
              is essential for the proliferation of a cell.

10   2.   A purified or isolated nucleic acid of Alloiococcus otitidis comprising a
              fragment of one of odd numbered sequences set forth in Seq. ID Nos: 1 to
              Seq. ID Nos: 105 said fragment selected from the group consisting of
              fragments comprising at least 10, at least 20, at least 25, at least 30, at least
              50 and more than 50 consecutive nucleotides of one of one of odd numbered
15   sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

       3.   A purified or isolated antisense nucleic acid comprising a nucleotide
              sequence complementary to at least a portion of an intragenic sequence,
              intergenic sequence, sequences spanning at least a portion of two or more
20   genes, 5' noncoding region, or 3' noncoding region within an operon
              comprising a proliferation-required gene of Alloiococcus otitidis whose activity
              or expression is inhibited by an antisense nucleic acid and selected from one
              of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

25   4.   A purified or isolated nucleic acid comprising a nucleotide sequence having at
              least 70% identity to a nucleotide sequence selected from one of odd
              numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105,
              fragments comprising at least 25 consecutive nucleotides selected from one
              of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105,
30   the nucleotide sequences complementary to one of odd numbered sequences
              set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, and the sequences
              complementary to fragments comprising at least 25 consecutive nucleotides

of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

5.   A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of any one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

5.   A purified or isolated polypeptide of Alloiococcus otitidis comprising a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or a fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the said polypeptides.

6.   A purified or isolated *Alloiococcus otitidis* polypeptide comprising a amino acid sequence having at least 25% amino acid identity to a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or at least 25% amino acid identity to a fragment comprising at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

7.   A purified or isolated *Alloiococcus otitidis* polypeptide comprising selected from one of the even numbered sequences set forth in Seq. ID Nos: 2 to Seq. ID Nos: 106, wherein the polypeptide is essential for the proliferation of a cell.

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8.   A method of producing an *Alloiococcus otitidis* polypeptide comprising introducing into a cell a vector comprising a promoter operably linked to a nucleic acid comprising a nucleotide sequence encoding a polypeptide whose

5   expression is essential for the proliferation and viability of *Alloiococcus otitidis*, and which is inhibited by an antisense nucleic acid, and which is selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105.

10

9.   A method of inhibiting the proliferation of *Alloiococcus otitidis* in an individual comprising inhibiting the activity or reducing the amount of a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth

15   in Seq. ID Nos: 1 to Seq. ID Nos: 105 or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product.

10.   A method for identifying a compound which influences the activity of an
20   *Alloiococcus otitidis* gene product , which is required for proliferation, said gene product comprising a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, said method comprising:

25

(a)   contacting said gene product with a candidate compound; and

(b)   determining whether said compound influences the activity of said gene product.

30   11.   A method for identifying a compound or an antisense nucleic acid having the ability to reduce activity or level of a *Alloiococcus otitidis* gene product, which is required for proliferation, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid

comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, said method comprising the steps of:

 (a) contacting a target gene or RNA encoding said gene product with a candidate compound or antisense nucleic acid; and

 (b) measuring the activity of said target.

13. A method for inhibiting cellular proliferation of *Alloiococcus otitidis* comprising introducing an effective amount of a compound with activity against a gene whose activity or expression is essential for cellular proliferation, and which is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or a compound with activity against the product of said gene into a population of *Alloiococcus otitidis* cells expressing said gene.

13. A composition comprising an effective concentration of an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

14. A method for identifying a compound having the ability to inhibit proliferation of *Alloiococcus otitidis* cell comprising:

 (a) identifying a homologue of a gene or gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, in a test cell, wherein said test cell is not *Alloiococcus otitidis*;

 (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homologue in said test cell;

 (b) contacting said test cell with a sublethal level of said inhibitory nucleic acid, thus sensitizing said cell;

 (c) contacting the sensitized cell of step (c) with a compound; and

(d) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said inhibitory nucleic acid.

5   16.   A method for identifying a compound having activity against a biological pathway required for proliferation comprising:

(a) sensitizing a cell by providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required for proliferation, wherein the activity or expression

10   of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, in said cell to reduce the activity or amount of said gene product;

15   (a) contacting the sensitized cell with a compound; and

(b) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

20   17.   A method for identifying a compound having the ability to inhibit one of the *Alloiococcus otitidis* polypeptides encoded by a polynucleotide selected from one of odd numbered sequences set forth in Seq. ID Nos: 1 to Seq. ID Nos: 105, and which is essential for cellular proliferation comprising:

(a) contacting a cell which expresses the polypeptide with the

25   compound; and

(b) determining whether said compound reduces proliferation of said contacted cell by acting on said gene product.

18.   A method for identifying a compound having the ability to inhibit one of the

30   purified and isolated *Alloiococcus otitidis* polypeptides selected from one of the even numbered sequences set forth in Seq. ID No.: 2 to Seq. ID No.: 106, and which is essential for cellular proliferation comprising:

-195-

(c) contacting the purified and isolated polypeptide with the compound
    in vitro in the presence or absence of a substrate, which is
    essential for the activity of the polypeptide; and

(d) determining the effect of the compound on the polypeptide by
    measuring the effect of the polypeptide on the substrate.

19.   A compound which interacts with an *Alloiococcus otitidis* polypeptide selected
      from one of the even numbered sequences set forth in Seq. ID No.: 2 to Seq.
      ID No.: 106 and inhibits its activity.

20.   A method for manufacturing an antimicrobial compound comprising the steps
      of screening one or more candidate compounds to identify a compound that
      reduces the activity or level of an *Alloiococcus otitidis* polypeptide selected
      from one of the even numbered sequences set forth in Seq. ID No.: 2 to Seq.
      ID No.: 106, said polypeptide comprising a gene product whose activity or
      expression is inhibited by an antisense nucleic acid comprising a nucleotide
      sequence selected from one of the odd numbered sequences set forth in Seq.
      ID No.: 1 to Seq. ID No. 105; and manufacturing the compound so identified.

21.   A compound which inhibits proliferation of *Alloiococcus otitidis* by interacting
      with a gene encoding a polypeptide that is required for proliferation or with a
      polypeptide required for proliferation, wherein said polypeptide is selected
      from the group consisting of a gene product having at least 70% nucleotide
      sequence identity from one of the odd numbered sequences set forth in Seq.
      ID No.: 1 to Seq. ID No. 105, polypeptide encoded by a nucleic acid having at
      least 70% nucleotide sequence identity to a nucleic acid encoding a
      polypeptide whose expression is inhibited by an antisense nucleic acid
      comprising a nucleotide sequence selected from one of the odd numbered
      sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105, a polypeptide
      having at least 25% amino acid identity to a gene product whose expression
      is inhibited by an antisense nucleic acid comprising a nucleotide sequence
      selected one of the odd numbered sequences set forth in Seq. ID No.: 1 to

Seq. ID No. 105, a polypeptide encoded by a nucleic acid comprising a
nucleotide sequence which hybridizes to a nucleic acid selected from one of
the odd numbered sequences set forth in Seq. ID No.: 1 to Seq. ID No. 105
under stringent conditions, a gene product encoded by a nucleic acid

5   comprising a nucleotide sequence which hybridizes to a nucleic acid selected
from one of the odd numbered sequences set forth in Seq. ID No.: 1 to Seq.
ID No. 105 under moderate conditions, and a gene product whose activity
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10   Seq. ID No.: 1 to Seq. ID No. 105.

SEQUENCE LISTING

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Gly Tyr Lys Gln Ala His Leu Leu Asn Asp Ala Tyr Asn Ala Ser Pro
            325             330             335

Thr Ser Met Lys Ala Val Leu Asp Tyr Phe Ser His Leu Asp Leu Asp
            340             345             350

Gly Glu Lys Ile Ala Val Leu Gly Asp Leu Arg Glu Leu Gly Ser Leu
        355             360             365

Ser Gly Gln Leu His Arg Ser Leu Ser Gln Ala Ile Asp Pro Lys Leu
    370             375             380

Leu Asp Arg Val Val Leu Tyr Gly Pro Glu Met Ala Ala Leu Tyr Gln
385             390             395             400

Val Leu Lys Ala Asp Phe Asp Pro Asp His Leu Thr Tyr Phe Pro Glu
            405             410             415

Asp Arg Lys Ala Leu Thr Asp Phe Leu Lys Glu Ile Met Gly Pro Ser
        420             425             430
```

```
Ser Tyr Leu Leu Leu Lys Ser Ser Leu Gly Thr Gly Leu Leu Glu Val
        435                 440                 445


Val Gln Ala Leu Ser Gln Lys Glu Asp Asp Glu Asn Gln Pro Leu Asp
    450                 455                 460
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<210> 5
<211> 1284
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (7)..(1284)
<223>

<400> 5

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gattgg atg aat ata atg aaa aaa cta atc atc aac ggt ggc cgg acc        48
       Met Asn Ile Met Lys Lys Leu Ile Ile Asn Gly Gly Arg Thr
        1               5               10

ctc aag ggt gaa gtc acg gta tca ggg gcc aaa aat agt acg gtg gct      96
Leu Lys Gly Glu Val Thr Val Ser Gly Ala Lys Asn Ser Thr Val Ala
15                  20              25                  30

ctc att cca gca tct att tta gca gac agc ccg gta atc cta gag ggg     144
Leu Ile Pro Ala Ser Ile Leu Ala Asp Ser Pro Val Ile Leu Glu Gly
                35                  40                  45

gta ccc gat atc cag gat gtt cat tcc cta ctg gag att tta aat gaa     192
Val Pro Asp Ile Gln Asp Val His Ser Leu Leu Glu Ile Leu Asn Glu
            50                  55                  60

atg aat gtc aag acc gac ttt gac gga aac act ttg acc att gac cca     240
Met Asn Val Lys Thr Asp Phe Asp Gly Asn Thr Leu Thr Ile Asp Pro
            65                  70                  75

aga gaa atg gtc tct atc ccc atg cca agt ggt aag atc caa agc ttg     288
Arg Glu Met Val Ser Ile Pro Met Pro Ser Gly Lys Ile Gln Ser Leu
    80                  85                  90

cgg gct tcc tac tac ttt atg gga gcc ctc ttg gcc aaa ttc ggt aaa     336
Arg Ala Ser Tyr Tyr Phe Met Gly Ala Leu Leu Ala Lys Phe Gly Lys
95                  100                 105                 110

ggg gta gtc ggt ctt ccc ggt ggt tgc ttc ctg ggg cca cga ccc atc     384
Gly Val Val Gly Leu Pro Gly Gly Cys Phe Leu Gly Pro Arg Pro Ile
                115                 120                 125

gac caa cac ttg aaa ggc ttc cgc ctg ctt gga gca gat gtg gat aat     432
Asp Gln His Leu Lys Gly Phe Arg Leu Leu Gly Ala Asp Val Asp Asn
                130                 135                 140
```

```
gaa atg ggg gcc atg tac ctt aaa acc agt gat tca ggc cta gtg ggt        480
Glu Met Gly Ala Met Tyr Leu Lys Thr Ser Asp Ser Gly Leu Val Gly
        145                 150                 155

agt cgg att tac tta gat gtt gtt tcg att ggt gca acc att aat atc        528
Ser Arg Ile Tyr Leu Asp Val Val Ser Ile Gly Ala Thr Ile Asn Ile
        160                 165                 170

atg tta gcc gct gtt agg gcc caa ggt cgg acg gtc att gag aat gcg        576
Met Leu Ala Ala Val Arg Ala Gln Gly Arg Thr Val Ile Glu Asn Ala
175                 180                 185                 190

gcc cga gaa cca gaa att att gat gtt gcc acc ctc ttg aac aag atg        624
Ala Arg Glu Pro Glu Ile Ile Asp Val Ala Thr Leu Leu Asn Lys Met
                195                 200                 205

ggg gct aaa ata cgt ggg gct ggc act gat atg atc cgg att gaa ggg        672
Gly Ala Lys Ile Arg Gly Ala Gly Thr Asp Met Ile Arg Ile Glu Gly
                210                 215                 220

gtt gac cag ctg act ggc tgc cag cac tcc atc atc ccc gac cgg att        720
Val Asp Gln Leu Thr Gly Cys Gln His Ser Ile Ile Pro Asp Arg Ile
        225                 230                 235

gaa gct ggg acc tac ctg gct att gca gcg gca gct ggg gag gat gtc        768
Glu Ala Gly Thr Tyr Leu Ala Ile Ala Ala Ala Ala Gly Glu Asp Val
        240                 245                 250

ctg gta aac aat gtt ata gtt gaa cat att gat agt tta att gcc aaa        816
Leu Val Asn Asn Val Ile Val Glu His Ile Asp Ser Leu Ile Ala Lys
255                 260                 265                 270

ctc gac gaa att ggt att gac ctg gac atc ggc gaa gac agt atc cgg        864
Leu Asp Glu Ile Gly Ile Asp Leu Asp Ile Gly Glu Asp Ser Ile Arg
                275                 280                 285

gtg aaa gcc ccc agt aaa cct ttg cag cct gtt acc atc aaa acc ctg        912
Val Lys Ala Pro Ser Lys Pro Leu Gln Pro Val Thr Ile Lys Thr Leu
                290                 295                 300

cct tac cct ggt ttt gcc act gac ctc cag cag ccc atc acc cct ctc        960
Pro Tyr Pro Gly Phe Ala Thr Asp Leu Gln Gln Pro Ile Thr Pro Leu
                305                 310                 315

ttg ctt ctg gcc aaa ggg gag tcc gtt atc acc gat acc atc tat cct       1008
Leu Leu Leu Ala Lys Gly Glu Ser Val Ile Thr Asp Thr Ile Tyr Pro
        320                 325                 330

aaa cgg gtt aag cac atc cct gag ctg gaa cgg atg ggg gcc aat atc       1056
Lys Arg Val Lys His Ile Pro Glu Leu Glu Arg Met Gly Ala Asn Ile
335                 340                 345                 350

cgg gtc gaa agc gat atc atc ctc att gaa ggt ggc cac ccc ctc aag       1104
Arg Val Glu Ser Asp Ile Ile Leu Ile Glu Gly Gly His Pro Leu Lys
                355                 360                 365
```

```
ggg gca gaa gtg gaa gcc agt gat tta aga gcc ggg gct tgc ttg att    1152
Gly Ala Glu Val Glu Ala Ser Asp Leu Arg Ala Gly Ala Cys Leu Ile
            370             375             380

aat gca ggt ttg atc gcg gaa ggt cag acg gaa att act ggc gtt gac    1200
Asn Ala Gly Leu Ile Ala Glu Gly Gln Thr Glu Ile Thr Gly Val Asp
            385             390             395

aaa att cta aga ggc tac tct cat att gtt gaa aaa ctc aat gac cta    1248
Lys Ile Leu Arg Gly Tyr Ser His Ile Val Glu Lys Leu Asn Asp Leu
            400             405             410

ggc gca gat gtt tat atg caa gag ggg gaa gac tga                    1284
Gly Ala Asp Val Tyr Met Gln Glu Gly Glu Asp
415             420             425
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<210> 6
<211> 425
<212> PRT
<213> Alloiococcus otitidis

<400> 6

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Met Asn Ile Met Lys Lys Leu Ile Ile Asn Gly Gly Arg Thr Leu Lys
1               5               10              15


Gly Glu Val Thr Val Ser Gly Ala Lys Asn Ser Thr Val Ala Leu Ile
                20              25              30


Pro Ala Ser Ile Leu Ala Asp Ser Pro Val Ile Leu Glu Gly Val Pro
            35              40              45


Asp Ile Gln Asp Val His Ser Leu Leu Glu Ile Leu Asn Glu Met Asn
        50              55              60


Val Lys Thr Asp Phe Asp Gly Asn Thr Leu Thr Ile Asp Pro Arg Glu
65              70              75              80


Met Val Ser Ile Pro Met Pro Ser Gly Lys Ile Gln Ser Leu Arg Ala
            85              90              95


Ser Tyr Tyr Phe Met Gly Ala Leu Leu Ala Lys Phe Gly Lys Gly Val
            100             105             110


Val Gly Leu Pro Gly Gly Cys Phe Leu Gly Pro Arg Pro Ile Asp Gln
            115             120             125


His Leu Lys Gly Phe Arg Leu Leu Gly Ala Asp Val Asp Asn Glu Met
        130             135             140
```

```
Gly Ala Met Tyr Leu Lys Thr Ser Asp Ser Gly Leu Val Gly Ser Arg
145                 150                 155                 160

Ile Tyr Leu Asp Val Val Ser Ile Gly Ala Thr Ile Asn Ile Met Leu
                165                 170                 175

Ala Ala Val Arg Ala Gln Gly Arg Thr Val Ile Glu Asn Ala Ala Arg
                180                 185                 190

Glu Pro Glu Ile Ile Asp Val Ala Thr Leu Leu Asn Lys Met Gly Ala
        195                 200                 205

Lys Ile Arg Gly Ala Gly Thr Asp Met Ile Arg Ile Glu Gly Val Asp
    210                 215                 220

Gln Leu Thr Gly Cys Gln His Ser Ile Ile Pro Asp Arg Ile Glu Ala
225                 230                 235                 240

Gly Thr Tyr Leu Ala Ile Ala Ala Ala Gly Glu Asp Val Leu Val
                245                 250                 255

Asn Asn Val Ile Val Glu His Ile Asp Ser Leu Ile Ala Lys Leu Asp
                260                 265                 270

Glu Ile Gly Ile Asp Leu Asp Ile Gly Glu Asp Ser Ile Arg Val Lys
        275                 280                 285

Ala Pro Ser Lys Pro Leu Gln Pro Val Thr Ile Lys Thr Leu Pro Tyr
    290                 295                 300

Pro Gly Phe Ala Thr Asp Leu Gln Gln Pro Ile Thr Pro Leu Leu Leu
305                 310                 315                 320

Leu Ala Lys Gly Glu Ser Val Ile Thr Asp Thr Ile Tyr Pro Lys Arg
                325                 330                 335

Val Lys His Ile Pro Glu Leu Glu Arg Met Gly Ala Asn Ile Arg Val
        340                 345                 350

Glu Ser Asp Ile Ile Leu Ile Glu Gly Gly His Pro Leu Lys Gly Ala
        355                 360                 365
```

Glu Val Glu Ala Ser Asp Leu Arg Ala Gly Ala Cys Leu Ile Asn Ala
    370   375   380

Gly Leu Ile Ala Glu Gly Gln Thr Glu Ile Thr Gly Val Asp Lys Ile
385   390   395   400

Leu Arg Gly Tyr Ser His Ile Val Glu Lys Leu Asn Asp Leu Gly Ala
                405   410   415

Asp Val Tyr Met Gln Glu Gly Glu Asp
            420   425

<210> 7
<211> 612
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (4)..(612)
<223>

<400> 7
ctt ttg cat aga caa gac ttg aat cgt gaa agg aag tca gat gtg gaa   48
    Met His Arg Gln Asp Leu Asn Arg Glu Arg Lys Ser Asp Val Glu
    1   5   10   15

tta aaa gag ttt gat gga aag aaa aaa gaa gaa cta gcc atg att gat   96
Leu Lys Glu Phe Asp Gly Lys Lys Lys Glu Glu Leu Ala Met Ile Asp
                20   25   30

gtg gcc aag gcc att tta gac cag gtc cat gac ttg atg cac ttc aac   144
Val Ala Lys Ala Ile Leu Asp Gln Val His Asp Leu Met His Phe Asn
                35   40   45

gac ctc ttg agt gaa gtg tct gaa tat cta gac ttg tca gat gac gag   192
Asp Leu Leu Ser Glu Val Ser Glu Tyr Leu Asp Leu Ser Asp Asp Glu
        50   55   60

atc gaa agc ggt atg ggc caa ttt tac acc gat tta aat att gac ggt   240
Ile Glu Ser Gly Met Gly Gln Phe Tyr Thr Asp Leu Asn Ile Asp Gly
    65   70   75

cgc ttc atc tct tta ggc gac aac cat tgg ggc tta cgt gaa tgg tat   288
Arg Phe Ile Ser Leu Gly Asp Asn His Trp Gly Leu Arg Glu Trp Tyr
80   85   90   95

cca gtc gat tct atc gat gaa gag ttg acc cac gac aat gac ctg gag   336
Pro Val Asp Ser Ile Asp Glu Glu Leu Thr His Asp Asn Asp Leu Glu
                100   105   110

aag gtc aca ccc aag cag gcg gaa gac ggc ttt gat gac tta gag cat   384

```
Lys Val Thr Pro Lys Gln Ala Glu Asp Gly Phe Asp Asp Leu Glu His
            115                 120                 125

gtc gaa aaa gaa gtg atg gat gac gca aaa gaa gaa tta gat gac cag    432
Val Glu Lys Glu Val Met Asp Asp Ala Lys Glu Glu Leu Asp Asp Gln
        130             135                 140

gcc gtc aat gaa gat gaa gaa aat gtt gct cca gat gaa atc acc gac    480
Ala Val Asn Glu Asp Glu Glu Asn Val Ala Pro Asp Glu Ile Thr Asp
    145                 150                 155

gat gga gat gaa gac aag ctg gat gaa tac tct agc gat atc gaa gac    528
Asp Gly Asp Glu Asp Lys Leu Asp Glu Tyr Ser Ser Asp Ile Glu Asp
160                 165                 170                 175

ctc gaa gat gat cgt aag gct agc caa gac aag ctg tcc att gtt gac    576
Leu Glu Asp Asp Arg Lys Ala Ser Gln Asp Lys Leu Ser Ile Val Asp
                180                 185                 190

gac gaa gat gtc tta aca aat gat gac gat gag taa                    612
Asp Glu Asp Val Leu Thr Asn Asp Asp Asp Glu
            195                 200
```

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<210> 8
<211> 202
<212> PRT
<213> Alloiococcus otitidis

<400> 8
Met His Arg Gln Asp Leu Asn Arg Glu Arg Lys Ser Asp Val Glu Leu
1               5                   10                  15


Lys Glu Phe Asp Gly Lys Lys Lys Glu Glu Leu Ala Met Ile Asp Val
            20                  25                  30


Ala Lys Ala Ile Leu Asp Gln Val His Asp Leu Met His Phe Asn Asp
    35                  40                  45


Leu Leu Ser Glu Val Ser Glu Tyr Leu Asp Leu Ser Asp Asp Glu Ile
    50                  55                  60


Glu Ser Gly Met Gly Gln Phe Tyr Thr Asp Leu Asn Ile Asp Gly Arg
65                  70                  75                  80


Phe Ile Ser Leu Gly Asp Asn His Trp Gly Leu Arg Glu Trp Tyr Pro
                85                  90                  95


Val Asp Ser Ile Asp Glu Glu Leu Thr His Asp Asn Asp Leu Glu Lys
            100                 105                 110
```

Val Thr Pro Lys Gln Ala Glu Asp Gly Phe Asp Asp Leu Glu His Val
      115   120   125

Glu Lys Glu Val Met Asp Asp Ala Lys Glu Glu Leu Asp Asp Gln Ala
      130   135   140

Val Asn Glu Asp Glu Glu Asn Val Ala Pro Asp Glu Ile Thr Asp Asp
145   150   155   160

Gly Asp Glu Asp Lys Leu Asp Glu Tyr Ser Ser Asp Ile Glu Asp Leu
                165   170   175

Glu Asp Asp Arg Lys Ala Ser Gln Asp Lys Leu Ser Ile Val Asp Asp
                180   185   190

Glu Asp Val Leu Thr Asn Asp Asp Asp Glu
          195   200

<210> 9
<211> 942
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (1)..(942)
<223>

<400> 9
atg atc gaa att gaa aag cca gta att gaa aca gta gag atc agt gaa   48
Met Ile Glu Ile Glu Lys Pro Val Ile Glu Thr Val Glu Ile Ser Glu
1   5   10   15

gat ggc aaa ttc ggt aag ttt gtt gtt gaa cca ttg gaa cgt ggt tat   96
Asp Gly Lys Phe Gly Lys Phe Val Val Glu Pro Leu Glu Arg Gly Tyr
            20   25   30

ggg act acc tta ggg aat tcc tta cgc cgc atc tta tta tca tca cta   144
Gly Thr Thr Leu Gly Asn Ser Leu Arg Arg Ile Leu Leu Ser Ser Leu
        35   40   45

ccg ggt gct gcg gtc acc aat att caa att gat ggt gtt ttg cat gag   192
Pro Gly Ala Ala Val Thr Asn Ile Gln Ile Asp Gly Val Leu His Glu
    50   55   60

ttt aca gct att gat ggt gtg gtt gaa gat gtg act tcc atc atc tta   240
Phe Thr Ala Ile Asp Gly Val Val Glu Asp Val Thr Ser Ile Ile Leu
65   70   75   80

aac ctg aaa aaa ctg gct tta aaa ctt cat act gaa gaa aca aaa aca   288

```
Asn Leu Lys Lys Leu Ala Leu Lys Leu His Thr Glu Glu Thr Lys Thr
            85                  90                  95

att gaa ttg gat att gaa ggc cct gct gaa gtg aca gca gct gat att    336
Ile Glu Leu Asp Ile Glu Gly Pro Ala Glu Val Thr Ala Ala Asp Ile
            100                 105                 110

att act gat agt gat gtt gag att atg aat cca gac cta tac ttg tgt    384
Ile Thr Asp Ser Asp Val Glu Ile Met Asn Pro Asp Leu Tyr Leu Cys
            115                 120                 125

act gtt tct gaa ggt ggt cat tta cac atc cgg atg gaa gca gaa act    432
Thr Val Ser Glu Gly Gly His Leu His Ile Arg Met Glu Ala Glu Thr
            130                 135                 140

ggt aga ggt tat gtg aat gca gag cac aac aag cat gat gat atg cca    480
Gly Arg Gly Tyr Val Asn Ala Glu His Asn Lys His Asp Asp Met Pro
145                 150                 155                 160

atc ggt gtt ttg cca att gat tca att tat acc cca att agc cgt gtc    528
Ile Gly Val Leu Pro Ile Asp Ser Ile Tyr Thr Pro Ile Ser Arg Val
                165                 170                 175

aac tat act gtt gaa gac acc cgc gtt ggt gaa cgc gag caa tat gat    576
Asn Tyr Thr Val Glu Asp Thr Arg Val Gly Glu Arg Glu Gln Tyr Asp
            180                 185                 190

aag tta acc ctg gat att tgg aca gat gga tcc atc tcc cca gag gat    624
Lys Leu Thr Leu Asp Ile Trp Thr Asp Gly Ser Ile Ser Pro Glu Asp
            195                 200                 205

ggc ttg agt cta gcg gct aag atc atg aat gaa cac ttg aac atc ttc    672
Gly Leu Ser Leu Ala Ala Lys Ile Met Asn Glu His Leu Asn Ile Phe
            210                 215                 220

atc aac tta act gag caa gca cgt gaa gcg gac att atg gtt gaa aaa    720
Ile Asn Leu Thr Glu Gln Ala Arg Glu Ala Asp Ile Met Val Glu Lys
225                 230                 235                 240

gaa gaa gac cag aaa gaa aaa atg ctt gag atg acc atc gaa gag ctt    768
Glu Glu Asp Gln Lys Glu Lys Met Leu Glu Met Thr Ile Glu Glu Leu
            245                 250                 255

gat tta tct gtt cgg tct tac aac tgt ttg aaa cgt gct ggc atc aat    816
Asp Leu Ser Val Arg Ser Tyr Asn Cys Leu Lys Arg Ala Gly Ile Asn
            260                 265                 270

act gtc caa gaa cta acg gac aaa act gaa ccg gaa atg atg aaa gtt    864
Thr Val Gln Glu Leu Thr Asp Lys Thr Glu Pro Glu Met Met Lys Val
            275                 280                 285

cgc aat ctc gga cgt aag tca tta gaa gaa gtt aaa aac aag ctt gat    912
Arg Asn Leu Gly Arg Lys Ser Leu Glu Glu Val Lys Asn Lys Leu Asp
            290                 295                 300

gac tta gac cta agc ttg aaa gaa gaa tag                            942
Asp Leu Asp Leu Ser Leu Lys Glu Glu
```

305   310

<210> 10
<211> 313
<212> PRT
<213> Alloiococcus otitidis

<400> 10
Met Ile Glu Ile Glu Lys Pro Val Ile Glu Thr Val Glu Ile Ser Glu
1   5   10   15

Asp Gly Lys Phe Gly Lys Phe Val Val Glu Pro Leu Glu Arg Gly Tyr
            20   25   30

Gly Thr Thr Leu Gly Asn Ser Leu Arg Arg Ile Leu Leu Ser Ser Leu
            35   40   45

Pro Gly Ala Ala Val Thr Asn Ile Gln Ile Asp Gly Val Leu His Glu
    50   55   60

Phe Thr Ala Ile Asp Gly Val Val Glu Asp Val Thr Ser Ile Ile Leu
65   70   75   80

Asn Leu Lys Lys Leu Ala Leu Lys Leu His Thr Glu Glu Thr Lys Thr
                85   90   95

Ile Glu Leu Asp Ile Glu Gly Pro Ala Glu Val Thr Ala Ala Asp Ile
            100   105   110

Ile Thr Asp Ser Asp Val Glu Ile Met Asn Pro Asp Leu Tyr Leu Cys
        115   120   125

Thr Val Ser Glu Gly Gly His Leu His Ile Arg Met Glu Ala Glu Thr
    130   135   140

Gly Arg Gly Tyr Val Asn Ala Glu His Asn Lys His Asp Asp Met Pro
145   150   155   160

Ile Gly Val Leu Pro Ile Asp Ser Ile Tyr Thr Pro Ile Ser Arg Val
            165   170   175

Asn Tyr Thr Val Glu Asp Thr Arg Val Gly Glu Arg Glu Gln Tyr Asp
            180   185   190

```
Lys Leu Thr Leu Asp Ile Trp Thr Asp Gly Ser Ile Ser Pro Glu Asp
        195               200             205
```

```
Gly Leu Ser Leu Ala Ala Lys Ile Met Asn Glu His Leu Asn Ile Phe
        210               215             220
```

```
Ile Asn Leu Thr Glu Gln Ala Arg Glu Ala Asp Ile Met Val Glu Lys
225               230             235               240
```

```
Glu Glu Asp Gln Lys Glu Lys Met Leu Glu Met Thr Ile Glu Glu Leu
            245             250               255
```

```
Asp Leu Ser Val Arg Ser Tyr Asn Cys Leu Lys Arg Ala Gly Ile Asn
            260             265             270
```

```
Thr Val Gln Glu Leu Thr Asp Lys Thr Glu Pro Glu Met Met Lys Val
        275               280             285
```

```
Arg Asn Leu Gly Arg Lys Ser Leu Glu Glu Val Lys Asn Lys Leu Asp
        290               295             300
```

```
Asp Leu Asp Leu Ser Leu Lys Glu Glu
305               310
```

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<210> 11
<211> 3681
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (22)..(3681)
<223>

<400> 11
aataaaggga ggtttgcccc c ttg gta gat gta aat aat ttt gaa agt att        51
                        Met Val Asp Val Asn Asn Phe Glu Ser Ile
                        1               5                   10

caa att gga ctg gct tca cca gag aaa atc cgt tca tgg tct cat ggt        99
Gln Ile Gly Leu Ala Ser Pro Glu Lys Ile Arg Ser Trp Ser His Gly
            15                  20                  25

gaa gtg aag aaa cct gaa acc att aac tac cgg aca tta aaa cct gaa       147
Glu Val Lys Lys Pro Glu Thr Ile Asn Tyr Arg Thr Leu Lys Pro Glu
            30                  35                  40

aaa gac ggt ttg ttc tgc gaa cgc att ttt ggc cca acc aag gac tat       195
Lys Asp Gly Leu Phe Cys Glu Arg Ile Phe Gly Pro Thr Lys Asp Tyr
```

```
                 45                    50                    55

gaa tgt gct tgc gga aaa tat aaa cga gtc cac tat aaa ggg ata gtt      243
Glu Cys Ala Cys Gly Lys Tyr Lys Arg Val His Tyr Lys Gly Ile Val
    60                  65                  70

tgt gac cgt tgc ggt gtt gaa gtc acc aag tcg agt gtc aga cga gaa      291
Cys Asp Arg Cys Gly Val Glu Val Thr Lys Ser Ser Val Arg Arg Glu
75                  80                  85                  90

cgc atg ggc cac ttg gaa tta gca gct cct gtc acc cac att tgg tac      339
Arg Met Gly His Leu Glu Leu Ala Ala Pro Val Thr His Ile Trp Tyr
                95                  100                 105

ttc aag ggt att cca agt cgg atg ggc ctt atc tta gat atg agc cca      387
Phe Lys Gly Ile Pro Ser Arg Met Gly Leu Ile Leu Asp Met Ser Pro
                110                 115                 120

aga tcc ttg gaa gaa att atc tat ttt gcc tct tat gtt gtt att gac      435
Arg Ser Leu Glu Glu Ile Ile Tyr Phe Ala Ser Tyr Val Val Ile Asp
            125                 130                 135

ggt ggg gat acc ccg ctt gaa cgc aaa cag ctc tta act gaa cgt gaa      483
Gly Gly Asp Thr Pro Leu Glu Arg Lys Gln Leu Leu Thr Glu Arg Glu
140                 145                 150

tac cgg gaa aac aaa agc aag tac ggc aat gaa ttc caa gct gaa att      531
Tyr Arg Glu Asn Lys Ser Lys Tyr Gly Asn Glu Phe Gln Ala Glu Ile
155                 160                 165                 170

gga gct gaa gct gtt cgg acc ttg cta aaa aat gtc gat ttg gaa caa      579
Gly Ala Glu Ala Val Arg Thr Leu Leu Lys Asn Val Asp Leu Glu Gln
                175                 180                 185

gaa gtt gct gac ctc aaa gaa atc tta gaa act gca act ggc caa aaa      627
Glu Val Ala Asp Leu Lys Glu Ile Leu Glu Thr Ala Thr Gly Gln Lys
            190                 195                 200

cgg acc cgg gct att cgt cgt tta gac att att gac tcc ttc aag tct      675
Arg Thr Arg Ala Ile Arg Arg Leu Asp Ile Ile Asp Ser Phe Lys Ser
            205                 210                 215

tcc aac aac aaa ccg gaa tgg atg gtc ttg gat gct att cca att atc      723
Ser Asn Asn Lys Pro Glu Trp Met Val Leu Asp Ala Ile Pro Ile Ile
    220                 225                 230

cca cct gaa ctc cgc cca atg gta caa cta gaa ggt ggc cgg ttt gca      771
Pro Pro Glu Leu Arg Pro Met Val Gln Leu Glu Gly Gly Arg Phe Ala
235                 240                 245                 250

acc agc gac ttg aac gac ttg tac cgc cgg gtg att aac cgg aac aac      819
Thr Ser Asp Leu Asn Asp Leu Tyr Arg Arg Val Ile Asn Arg Asn Asn
                255                 260                 265

cgg ttg aaa cgc ttg ctt gac ttg aat gcc ccc cac att atc gtc caa      867
Arg Leu Lys Arg Leu Leu Asp Leu Asn Ala Pro His Ile Ile Val Gln
            270                 275                 280
```

```
aat gaa aaa cgg atg ctg caa gaa gct gtt gac gcc ttg att gac aat      915
Asn Glu Lys Arg Met Leu Gln Glu Ala Val Asp Ala Leu Ile Asp Asn
        285                 290                 295

ggt cgt cgc ggt cgg gca gtc aac ggt cct ggt aac cgt ccg ctt aaa      963
Gly Arg Arg Gly Arg Ala Val Asn Gly Pro Gly Asn Arg Pro Leu Lys
        300                 305                 310

tct ctt tct cac atg ttg aaa ggg aaa caa ggg cgc ttc cgt cag aac     1011
Ser Leu Ser His Met Leu Lys Gly Lys Gln Gly Arg Phe Arg Gln Asn
315                 320                 325                 330

cta cta ggg aaa cgg gtt gac tac tct ggc cgg tct gtc att gtt gtt     1059
Leu Leu Gly Lys Arg Val Asp Tyr Ser Gly Arg Ser Val Ile Val Val
            335                 340                 345

ggg cca acc ctt aaa atg tac caa tgt ggt cta ccg aaa gaa atg gcc     1107
Gly Pro Thr Leu Lys Met Tyr Gln Cys Gly Leu Pro Lys Glu Met Ala
                350                 355                 360

atc gaa ctc ttc aaa cct ttt gtc atg cgg gag cta gtt gag cga gat     1155
Ile Glu Leu Phe Lys Pro Phe Val Met Arg Glu Leu Val Glu Arg Asp
            365                 370                 375

att gca aat aac att aaa aat gcc aaa cga aaa gtg gaa cgg atg gaa     1203
Ile Ala Asn Asn Ile Lys Asn Ala Lys Arg Lys Val Glu Arg Met Glu
        380                 385                 390

gat gat gtc tgg cct gtt tta gaa gat gtc att aaa gaa cac cct gtc     1251
Asp Asp Val Trp Pro Val Leu Glu Asp Val Ile Lys Glu His Pro Val
395                 400                 405                 410

ctc tta aac cgg gcc cct acc ctt cac cgg cta ggg atc caa gcc ttt     1299
Leu Leu Asn Arg Ala Pro Thr Leu His Arg Leu Gly Ile Gln Ala Phe
            415                 420                 425

gaa cct gtc ctt gtc aat ggg aag gct att cgc tta cac cca ctc gct     1347
Glu Pro Val Leu Val Asn Gly Lys Ala Ile Arg Leu His Pro Leu Ala
            430                 435                 440

tgt gaa gcc tac aat gct gac ttt gac gga gac caa atg gct gtc cac     1395
Cys Glu Ala Tyr Asn Ala Asp Phe Asp Gly Asp Gln Met Ala Val His
                445                 450                 455

gta ccc ctc agt gat gaa gcc cag gca gaa gcc cgc atc tta atg ctg     1443
Val Pro Leu Ser Asp Glu Ala Gln Ala Glu Ala Arg Ile Leu Met Leu
        460                 465                 470

ggt gcc caa aat atc tta aac cct aaa gat ggt caa cca gtc gtt acc     1491
Gly Ala Gln Asn Ile Leu Asn Pro Lys Asp Gly Gln Pro Val Val Thr
475                 480                 485                 490

cct tcc caa gac atg gtc cta ggg aac tac tac cta acc atg gaa gaa     1539
Pro Ser Gln Asp Met Val Leu Gly Asn Tyr Tyr Leu Thr Met Glu Glu
            495                 500                 505
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gaa ggt aaa att ggt gaa gga act gtc ttc tcc agt gct tct gag gct        1587
Glu Gly Lys Ile Gly Glu Gly Thr Val Phe Ser Ser Ala Ser Glu Ala
            510             515             520

atc caa gcc tac caa aca ggc tat gtc cac ctc cac acc cgg gtt gcg        1635
Ile Gln Ala Tyr Gln Thr Gly Tyr Val His Leu His Thr Arg Val Ala
            525             530             535

atc cgt gcg gtg gac tta ccg gac aaa cct ttt act gac tgg cag aaa        1683
Ile Arg Ala Val Asp Leu Pro Asp Lys Pro Phe Thr Asp Trp Gln Lys
            540             545             550

gac aag tac ttg att acc aca gtc ggt aag att atc ttt aat gaa att        1731
Asp Lys Tyr Leu Ile Thr Thr Val Gly Lys Ile Ile Phe Asn Glu Ile
555             560             565             570

atg cca gca gaa ttt cca ttc ttg aac gaa cca tct aag gtt aac ctg        1779
Met Pro Ala Glu Phe Pro Phe Leu Asn Glu Pro Ser Lys Val Asn Leu
            575             580             585

gaa cag caa acc cca gac aag tac ttt gtc gac cgg ggc caa aac ttg        1827
Glu Gln Gln Thr Pro Asp Lys Tyr Phe Val Asp Arg Gly Gln Asn Leu
            590             595             600

aaa gac ctt att gcc gac cgt cct tta gtt cag cct ttc aaa aaa caa        1875
Lys Asp Leu Ile Ala Asp Arg Pro Leu Val Gln Pro Phe Lys Lys Gln
            605             610             615

gac ctg tcc aac att atc gcc gaa gtc ttt aat aac ttc caa gtg acc        1923
Asp Leu Ser Asn Ile Ile Ala Glu Val Phe Asn Asn Phe Gln Val Thr
            620             625             630

gaa acc tct aaa atg ttg gac cgc atg aag aac ttg ggc tac aag tac        1971
Glu Thr Ser Lys Met Leu Asp Arg Met Lys Asn Leu Gly Tyr Lys Tyr
635             640             645             650

tct acc cgg tct ggt att act gtt ggg att gct gac gtt tca gtc cta        2019
Ser Thr Arg Ser Gly Ile Thr Val Gly Ile Ala Asp Val Ser Val Leu
            655             660             665

gaa gct aaa cca gaa atc ctg aaa gaa gcc cac gcc aag gtt gat aaa        2067
Glu Ala Lys Pro Glu Ile Leu Lys Glu Ala His Ala Lys Val Asp Lys
            670             675             680

atc aat gcc acc cac cgc cgc ggt tta att act gaa gaa gag cgt tac        2115
Ile Asn Ala Thr His Arg Arg Gly Leu Ile Thr Glu Glu Glu Arg Tyr
            685             690             695

gac aac gtt atc gat gtc tgg caa aag gct aag gat gaa att caa gat        2163
Asp Asn Val Ile Asp Val Trp Gln Lys Ala Lys Asp Glu Ile Gln Asp
            700             705             710

gcc ttg atg gat tcc ctt gac cca aga aat aac atc ttt atg atg tca        2211
Ala Leu Met Asp Ser Leu Asp Pro Arg Asn Asn Ile Phe Met Met Ser
715             720             725             730

gac tct ggt gcc cgt ggg aat att tcc aac ttc acc caa cta gcc ggt        2259
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Asp Ser Gly Ala Arg Gly Asn Ile Ser Asn Phe Thr Gln Leu Ala Gly
                735                 740                 745

atg cgt ggt ttg atg gca gca cca agt ggt gag atc atg gaa ttg ccg      2307
Met Arg Gly Leu Met Ala Ala Pro Ser Gly Glu Ile Met Glu Leu Pro
            750                 755                 760

atc acg tct aac ttc cgt gaa ggc ctg tct gtc tta gag atg ttt att      2355
Ile Thr Ser Asn Phe Arg Glu Gly Leu Ser Val Leu Glu Met Phe Ile
            765                 770                 775

tcc acc cac ggt gcc cgt aaa ggc atg acc gat acc gcc ctt aaa act      2403
Ser Thr His Gly Ala Arg Lys Gly Met Thr Asp Thr Ala Leu Lys Thr
        780                 785                 790

gcc gac tct ggt tac ttg acc aga cgt ttg gtt gat gtt gcc caa gac      2451
Ala Asp Ser Gly Tyr Leu Thr Arg Arg Leu Val Asp Val Ala Gln Asp
795                 800                 805                 810

gtc atc atc cga gaa gaa gac tgt ggc act aaa cgt ggc ctt aaa gtt      2499
Val Ile Ile Arg Glu Glu Asp Cys Gly Thr Lys Arg Gly Leu Lys Val
                815                 820                 825

tct gcc atc caa gta gga aat gaa cag att gaa agc ttg tct gac cgt      2547
Ser Ala Ile Gln Val Gly Asn Glu Gln Ile Glu Ser Leu Ser Asp Arg
            830                 835                 840

atc ttg ggt cgt tat gcc caa gaa acc gtc acc cac ccc gaa act ggt      2595
Ile Leu Gly Arg Tyr Ala Gln Glu Thr Val Thr His Pro Glu Thr Gly
            845                 850                 855

gaa gtc att gtt cac aag gat gaa ttg att gat gaa ggc aaa acc cga      2643
Glu Val Ile Val His Lys Asp Glu Leu Ile Asp Glu Gly Lys Thr Arg
        860                 865                 870

aaa att gtc gat gcc ggt att gaa gaa gtt act atc cgg tct gcc ttc      2691
Lys Ile Val Asp Ala Gly Ile Glu Glu Val Thr Ile Arg Ser Ala Phe
875                 880                 885                 890

tgc tgc aac acc aac cac ggt gtc tgc aag cac tgc tat ggc cgt aac      2739
Cys Cys Asn Thr Asn His Gly Val Cys Lys His Cys Tyr Gly Arg Asn
                895                 900                 905

ttg gca act ggc cgg gaa gtt gaa gtt ggt gaa gca gtt gga act atc      2787
Leu Ala Thr Gly Arg Glu Val Glu Val Gly Glu Ala Val Gly Thr Ile
            910                 915                 920

gct gcc caa tcc att ggg gaa ccc ggt acc caa ttg acc atg cgg acc      2835
Ala Ala Gln Ser Ile Gly Glu Pro Gly Thr Gln Leu Thr Met Arg Thr
            925                 930                 935

ttc cac act ggt ggg gtc gct ggg gac gac atc acc caa ggt cta cca      2883
Phe His Thr Gly Gly Val Ala Gly Asp Asp Ile Thr Gln Gly Leu Pro
        940                 945                 950

cgg gtt caa gaa atc ttt gaa gcc cgc cat ccg aaa ggg caa gcc acc      2931
Arg Val Gln Glu Ile Phe Glu Ala Arg His Pro Lys Gly Gln Ala Thr
```

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      955                     960                     965                     970

att aca gaa gtg aat ggt caa atc caa gag atc gtt gaa gac cct gaa    2979
Ile Thr Glu Val Asn Gly Gln Ile Gln Glu Ile Val Glu Asp Pro Glu
                    975                 980                 985

gaa cgc act aag acc gtc act gtt aag ggg aat gtt gac caa cgt gac    3027
Glu Arg Thr Lys Thr Val Thr Val Lys Gly Asn Val Asp Gln Arg Asp
                990                 995                 1000

tac tcc ttg cca atc aat gcc cgg atg aag gtt gaa gtt ggg gat tat    3075
Tyr Ser Leu Pro Ile Asn Ala Arg Met Lys Val Glu Val Gly Asp Tyr
            1005                1010                1015

gtt gaa cga ggc gat gct cta aac gag ggg tct att gat ccg aaa gag    3123
Val Glu Arg Gly Asp Ala Leu Asn Glu Gly Ser Ile Asp Pro Lys Glu
        1020                1025                1030

tta ctc gcg gtg agt gat atg atg aaa ttg cag aaa tac ctc ttg caa    3171
Leu Leu Ala Val Ser Asp Met Met Lys Leu Gln Lys Tyr Leu Leu Gln
  1035                1040                1045                1050

gaa gtc caa tac gct tac cgg tct caa ggg gtc gaa att ggt gac aag    3219
Glu Val Gln Tyr Ala Tyr Arg Ser Gln Gly Val Glu Ile Gly Asp Lys
            1055                1060                1065

cac gtg gag gtt atg gtg cga caa atg ctc cgt aaa gtc cgt gtc ttg    3267
His Val Glu Val Met Val Arg Gln Met Leu Arg Lys Val Arg Val Leu
        1070                1075                1080

caa cca ggg gac act gat atc ctg cct ggt acc atg att gac ctc cac    3315
Gln Pro Gly Asp Thr Asp Ile Leu Pro Gly Thr Met Ile Asp Leu His
        1085                1090                1095

gac ttc aag gaa cgc aac caa gaa acc ttg atg tcc ggt ggc caa ccc    3363
Asp Phe Lys Glu Arg Asn Gln Glu Thr Leu Met Ser Gly Gly Gln Pro
    1100                1105                1110

gca act gct aga ctg gtc cta ctg ggt att acc aag gcc tcc ctt gaa    3411
Ala Thr Ala Arg Leu Val Leu Leu Gly Ile Thr Lys Ala Ser Leu Glu
1115                1120                1125                1130

acc aac tct ttc ttg tct gca gct tcc ttc caa gaa acc acc cgg gtc    3459
Thr Asn Ser Phe Leu Ser Ala Ala Ser Phe Gln Glu Thr Thr Arg Val
            1135                1140                1145

ctc acc gat gca gct att cgc ggt aaa gtt gat gac ctg gtt ggc ttg    3507
Leu Thr Asp Ala Ala Ile Arg Gly Lys Val Asp Asp Leu Val Gly Leu
            1150                1155                1160

aaa gaa aat gtt att atc ggt aaa tcc atc cca gct ggt act ggt atg    3555
Lys Glu Asn Val Ile Ile Gly Lys Ser Ile Pro Ala Gly Thr Gly Met
        1165                1170                1175

aga gcc tac agt aat att gaa cct aaa aaa gtt ggt gtc gtt agc gaa    3603
Arg Ala Tyr Ser Asn Ile Glu Pro Lys Lys Val Gly Val Val Ser Glu
    1180                1185                1190
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aat gtc tac agc atc aat gaa gaa gac caa gtc agt caa gaa gaa aac    3651
Asn Val Tyr Ser Ile Asn Glu Glu Asp Gln Val Ser Gln Glu Glu Asn
1195                1200              1205              1210

cga gaa act gaa gaa act agc gag aaa taa                            3681
Arg Glu Thr Glu Glu Thr Ser Glu Lys
              1215
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<213> Alloiococcus otitidis

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Met Val Asp Val Asn Asn Phe Glu Ser Ile Gln Ile Gly Leu Ala Ser
1               5               10              15


Pro Glu Lys Ile Arg Ser Trp Ser His Gly Glu Val Lys Lys Pro Glu
            20              25              30


Thr Ile Asn Tyr Arg Thr Leu Lys Pro Glu Lys Asp Gly Leu Phe Cys
            35              40              45


Glu Arg Ile Phe Gly Pro Thr Lys Asp Tyr Glu Cys Ala Cys Gly Lys
    50              55              60


Tyr Lys Arg Val His Tyr Lys Gly Ile Val Cys Asp Arg Cys Gly Val
65              70              75              80


Glu Val Thr Lys Ser Ser Val Arg Arg Glu Arg Met Gly His Leu Glu
            85              90              95


Leu Ala Ala Pro Val Thr His Ile Trp Tyr Phe Lys Gly Ile Pro Ser
            100             105             110


Arg Met Gly Leu Ile Leu Asp Met Ser Pro Arg Ser Leu Glu Glu Ile
            115             120             125


Ile Tyr Phe Ala Ser Tyr Val Val Ile Asp Gly Gly Asp Thr Pro Leu
    130             135             140


Glu Arg Lys Gln Leu Leu Thr Glu Arg Glu Tyr Arg Glu Asn Lys Ser
145             150             155             160


Lys Tyr Gly Asn Glu Phe Gln Ala Glu Ile Gly Ala Glu Ala Val Arg
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              165   170   175

Thr Leu Leu Lys Asn Val Asp Leu Glu Gln Glu Val Ala Asp Leu Lys
        180   185   190

Glu Ile Leu Glu Thr Ala Thr Gly Gln Lys Arg Thr Arg Ala Ile Arg
        195   200   205

Arg Leu Asp Ile Ile Asp Ser Phe Lys Ser Ser Asn Asn Lys Pro Glu
        210   215   220

Trp Met Val Leu Asp Ala Ile Pro Ile Ile Pro Pro Glu Leu Arg Pro
225   230   235   240

Met Val Gln Leu Glu Gly Gly Arg Phe Ala Thr Ser Asp Leu Asn Asp
                245   250   255

Leu Tyr Arg Arg Val Ile Asn Arg Asn Asn Arg Leu Lys Arg Leu Leu
                260   265   270

Asp Leu Asn Ala Pro His Ile Ile Val Gln Asn Glu Lys Arg Met Leu
        275   280   285

Gln Glu Ala Val Asp Ala Leu Ile Asp Asn Gly Arg Arg Gly Arg Ala
        290   295   300

Val Asn Gly Pro Gly Asn Arg Pro Leu Lys Ser Leu Ser His Met Leu
305   310   315   320

Lys Gly Lys Gln Gly Arg Phe Arg Gln Asn Leu Leu Gly Lys Arg Val
                325   330   335

Asp Tyr Ser Gly Arg Ser Val Ile Val Val Gly Pro Thr Leu Lys Met
                340   345   350

Tyr Gln Cys Gly Leu Pro Lys Glu Met Ala Ile Glu Leu Phe Lys Pro
                355   360   365

Phe Val Met Arg Glu Leu Val Glu Arg Asp Ile Ala Asn Asn Ile Lys
        370   375   380

Asn Ala Lys Arg Lys Val Glu Arg Met Glu Asp Asp Val Trp Pro Val
385   390   395   400
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Leu Glu Asp Val Ile Lys Glu His Pro Val Leu Leu Asn Arg Ala Pro
405 410 415

Thr Leu His Arg Leu Gly Ile Gln Ala Phe Glu Pro Val Leu Val Asn
420 425 430

Gly Lys Ala Ile Arg Leu His Pro Leu Ala Cys Glu Ala Tyr Asn Ala
435 440 445

Asp Phe Asp Gly Asp Gln Met Ala Val His Val Pro Leu Ser Asp Glu
450 455 460

Ala Gln Ala Glu Ala Arg Ile Leu Met Leu Gly Ala Gln Asn Ile Leu
465 470 475 480

Asn Pro Lys Asp Gly Gln Pro Val Val Thr Pro Ser Gln Asp Met Val
485 490 495

Leu Gly Asn Tyr Tyr Leu Thr Met Glu Glu Glu Gly Lys Ile Gly Glu
500 505 510

Gly Thr Val Phe Ser Ser Ala Ser Glu Ala Ile Gln Ala Tyr Gln Thr
515 520 525

Gly Tyr Val His Leu His Thr Arg Val Ala Ile Arg Ala Val Asp Leu
530 535 540

Pro Asp Lys Pro Phe Thr Asp Trp Gln Lys Asp Lys Tyr Leu Ile Thr
545 550 555 560

Thr Val Gly Lys Ile Ile Phe Asn Glu Ile Met Pro Ala Glu Phe Pro
565 570 575

Phe Leu Asn Glu Pro Ser Lys Val Asn Leu Glu Gln Gln Thr Pro Asp
580 585 590

Lys Tyr Phe Val Asp Arg Gly Gln Asn Leu Lys Asp Leu Ile Ala Asp
595 600 605

Arg Pro Leu Val Gln Pro Phe Lys Lys Gln Asp Leu Ser Asn Ile Ile
610 615 620

Ala Glu Val Phe Asn Asn Phe Gln Val Thr Glu Thr Ser Lys Met Leu
625   630   635   640

Asp Arg Met Lys Asn Leu Gly Tyr Lys Tyr Ser Thr Arg Ser Gly Ile
                645   650   655

Thr Val Gly Ile Ala Asp Val Ser Val Leu Glu Ala Lys Pro Glu Ile
                660   665   670

Leu Lys Glu Ala His Ala Lys Val Asp Lys Ile Asn Ala Thr His Arg
                675   680   685

Arg Gly Leu Ile Thr Glu Glu Glu Arg Tyr Asp Asn Val Ile Asp Val
                690   695   700

Trp Gln Lys Ala Lys Asp Glu Ile Gln Asp Ala Leu Met Asp Ser Leu
705   710   715   720

Asp Pro Arg Asn Asn Ile Phe Met Met Ser Asp Ser Gly Ala Arg Gly
                725   730   735

Asn Ile Ser Asn Phe Thr Gln Leu Ala Gly Met Arg Gly Leu Met Ala
                740   745   750

Ala Pro Ser Gly Glu Ile Met Glu Leu Pro Ile Thr Ser Asn Phe Arg
                755   760   765

Glu Gly Leu Ser Val Leu Glu Met Phe Ile Ser Thr His Gly Ala Arg
                770   775   780

Lys Gly Met Thr Asp Thr Ala Leu Lys Thr Ala Asp Ser Gly Tyr Leu
785   790   795   800

Thr Arg Arg Leu Val Asp Val Ala Gln Asp Val Ile Ile Arg Glu Glu
                805   810   815

Asp Cys Gly Thr Lys Arg Gly Leu Lys Val Ser Ala Ile Gln Val Gly
                820   825   830

Asn Glu Gln Ile Glu Ser Leu Ser Asp Arg Ile Leu Gly Arg Tyr Ala
                835   840   845

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Gln Glu Thr Val Thr His Pro Glu Thr Gly Glu Val Ile Val His Lys
850                 855             860

Asp Glu Leu Ile Asp Glu Gly Lys Thr Arg Lys Ile Val Asp Ala Gly
865             870             875             880

Ile Glu Glu Val Thr Ile Arg Ser Ala Phe Cys Cys Asn Thr Asn His
                885             890         ..      895

Gly Val Cys Lys His Cys Tyr Gly Arg Asn Leu Ala Thr Gly Arg Glu
            900             905             910

Val Glu Val Gly Glu Ala Val Gly Thr Ile Ala Ala Gln Ser Ile Gly
        915         .       920             925

Glu Pro Gly Thr Gln Leu Thr Met Arg Thr Phe His Thr Gly Gly Val
    930             935             940

Ala Gly Asp Asp Ile Thr Gln Gly Leu Pro Arg Val Gln Glu Ile Phe
945             950             955             960

Glu Ala Arg His Pro Lys Gly Gln Ala Thr Ile Thr Glu Val Asn Gly
            965             970             975

Gln Ile Gln Glu Ile Val Glu Asp Pro Glu Glu Arg Thr Lys Thr Val
            980             985             990

Thr Val Lys Gly Asn Val Asp Gln Arg Asp Tyr Ser Leu Pro Ile Asn
        995             1000            1005

Ala Arg Met Lys Val Glu Val Gly Asp Tyr Val Glu Arg Gly Asp Ala
    1010            1015            1020

Leu Asn Glu Gly Ser Ile Asp Pro Lys Glu Leu Leu Ala Val Ser Asp
1025            1030            1035            1040

Met Met Lys Leu Gln Lys Tyr Leu Leu Gln Glu Val Gln Tyr Ala Tyr
            1045            1050            1055

Arg Ser Gln Gly Val Glu Ile Gly Asp Lys His Val Glu Val Met Val
            1060            1065            1070

Arg Gln Met Leu Arg Lys Val Arg Val Leu Gln Pro Gly Asp Thr Asp
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         1075              1080                1085
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Ile Leu Pro Gly Thr Met Ile Asp Leu His Asp Phe Lys Glu Arg Asn
    1090   1095   1100

Gln Glu Thr Leu Met Ser Gly Gly Gln Pro Ala Thr Ala Arg Leu Val
1105   1110   1115   1120

Leu Leu Gly Ile Thr Lys Ala Ser Leu Glu Thr Asn Ser Phe Leu Ser
              1125   1130   1135

Ala Ala Ser Phe Gln Glu Thr Thr Arg Val Leu Thr Asp Ala Ala Ile
              1140   1145   1150

Arg Gly Lys Val Asp Asp Leu Val Gly Leu Lys Glu Asn Val Ile Ile
         1155   1160   1165

Gly Lys Ser Ile Pro Ala Gly Thr Gly Met Arg Ala Tyr Ser Asn Ile
    1170   1175   1180

Glu Pro Lys Lys Val Gly Val Val Ser Glu Asn Val Tyr Ser Ile Asn
1185   1190   1195   1200

Glu Glu Asp Gln Val Ser Gln Glu Glu Asn Arg Glu Thr Glu Glu Thr
              1205   1210   1215

Ser Glu Lys

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<211> 3582
<212> DNA
<213> Alloiococcus otitidis

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<221> CDS
<222> (4)..(3582)
<223>

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       Met Asn Lys Leu Val Gly Lys Lys Val Asn Phe Gly Lys His Arg
       1               5               10              15

   gtt cgt aga agt tac tca cga atc aac gaa gta ctc gag ctc ccg aat       96
   Val Arg Arg Ser Tyr Ser Arg Ile Asn Glu Val Leu Glu Leu Pro Asn
                   20              25              30
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tta att gaa atc cag act gat tca tat gat tgg ttt tta gat gaa ggc        144
Leu Ile Glu Ile Gln Thr Asp Ser Tyr Asp Trp Phe Leu Asp Glu Gly
            35                  40                  45

ttg aag gaa atg ttt agt gat att tcc cca atc gat gat ttt tca ggc        192
Leu Lys Glu Met Phe Ser Asp Ile Ser Pro Ile Asp Asp Phe Ser Gly
            50                  55                  60

aat ttg tcc cta gaa ttt gtt gac tat aaa ttt tac gaa agc aag tat        240
Asn Leu Ser Leu Glu Phe Val Asp Tyr Lys Phe Tyr Glu Ser Lys Tyr
        65                  70                  75

act gtt gaa gaa gct aga gag cat gat gcg aac tat tct gcc ccc ctc        288
Thr Val Glu Glu Ala Arg Glu His Asp Ala Asn Tyr Ser Ala Pro Leu
80                  85                  90                  95

tac gtg aag tta cgt ttg atc aac aag gaa act ggt gaa gtc aag gaa        336
Tyr Val Lys Leu Arg Leu Ile Asn Lys Glu Thr Gly Glu Val Lys Glu
                100                 105                 110

caa gaa gtc ttc ttc ggt gac ttt ccg tta atg aca gaa caa ggg acc       384
Gln Glu Val Phe Phe Gly Asp Phe Pro Leu Met Thr Glu Gln Gly Thr
            115                 120                 125

ttt atc atc aac ggg gct gag cgg gtg att gtt tcc caa ctt gtc cgg       432
Phe Ile Ile Asn Gly Ala Glu Arg Val Ile Val Ser Gln Leu Val Arg
        130                 135                 140

tcg cct ggg gtt tat tac agt cca aaa gtt gag aaa aac ggc cgg gaa       480
Ser Pro Gly Val Tyr Tyr Ser Pro Lys Val Glu Lys Asn Gly Arg Glu
    145                 150                 155

ggt ttt tca acc gtt ctt atc cct aac cgg ggt gct tgg ctt gaa tac       528
Gly Phe Ser Thr Val Leu Ile Pro Asn Arg Gly Ala Trp Leu Glu Tyr
160                 165                 170                 175

gaa aca gat acc aaa ggc atc tcc aat gtt cga att gac cga acc cgt       576
Glu Thr Asp Thr Lys Gly Ile Ser Asn Val Arg Ile Asp Arg Thr Arg
                180                 185                 190

aaa att ccg atc act gtc ttg tta aga gct cta ggg att ggg tca gat       624
Lys Ile Pro Ile Thr Val Leu Leu Arg Ala Leu Gly Ile Gly Ser Asp
                195                 200                 205

gat gaa att att gac ctg atc ggc ttg aat gac agc ttg gaa gcc acc       672
Asp Glu Ile Ile Asp Leu Ile Gly Leu Asn Asp Ser Leu Glu Ala Thr
            210                 215                 220

ttg gaa aag gat gtc cac aag tct act tca gat tcc cgc gta gaa gaa       720
Leu Glu Lys Asp Val His Lys Ser Thr Ser Asp Ser Arg Val Glu Glu
    225                 230                 235

gcc ttg aaa gac ttg tat gaa cgc ttg cgt cca ggt gaa ccc aaa aca       768
Ala Leu Lys Asp Leu Tyr Glu Arg Leu Arg Pro Gly Glu Pro Lys Thr
240                 245                 250                 255

gct gaa tcc tct cgt aac ttg atc aat acc cgg ttc ttt gac cac aag       816
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                 Ala Glu Ser Ser Arg Asn Leu Ile Asn Thr Arg Phe Phe Asp His Lys
                             260                 265             270

cgt tac gac cta gcc tat gtt ggt cgc tac aag atg aac aaa aaa cta          864
Arg Tyr Asp Leu Ala Tyr Val Gly Arg Tyr Lys Met Asn Lys Lys Leu
            275                 280                 285

gac ctt aaa acc cgc ttg atg ggg act gtc ctt gcc gaa aac ctg gtt          912
Asp Leu Lys Thr Arg Leu Met Gly Thr Val Leu Ala Glu Asn Leu Val
            290                 295                 300

gat cct gaa gct ggc gag gtc tta gct gaa gaa ggt agt gaa gtg acc          960
Asp Pro Glu Ala Gly Glu Val Leu Ala Glu Glu Gly Ser Glu Val Thr
    305                 310                 315

cgg tct gtg atg gac aag ctt ggc cct tac ctt gac ggt gac atg aac        1008
Arg Ser Val Met Asp Lys Leu Gly Pro Tyr Leu Asp Gly Asp Met Asn
320                 325                 330                 335

caa gta acc att aac ccc tca gaa gaa gcg gtt atc cct gaa ccc att        1056
Gln Val Thr Ile Asn Pro Ser Glu Glu Ala Val Ile Pro Glu Pro Ile
                    340                 345                 350

gac cta caa att gtc aaa gtc tac tcc aaa gaa gat cca gac cgg atc        1104
Asp Leu Gln Ile Val Lys Val Tyr Ser Lys Glu Asp Pro Asp Arg Ile
                355                 360                 365

gtg aac atg atc ggc aac ggg cac cct gac aaa aag gcc aaa tgg att        1152
Val Asn Met Ile Gly Asn Gly His Pro Asp Lys Lys Ala Lys Trp Ile
            370                 375                 380

acc cct gct gac atg ata gcg gct atg agt tac ttc ttt aac ctc caa        1200
Thr Pro Ala Asp Met Ile Ala Ala Met Ser Tyr Phe Phe Asn Leu Gln
    385                 390                 395

gaa ggc att ggc gat gtt gac gat atc gac cac ttg ggt aac cgt cgg        1248
Glu Gly Ile Gly Asp Val Asp Asp Ile Asp His Leu Gly Asn Arg Arg
400                 405                 410                 415

atc cgg tca gtc gga gag ctt ttg caa aac caa ttc cga att ggg ctc        1296
Ile Arg Ser Val Gly Glu Leu Leu Gln Asn Gln Phe Arg Ile Gly Leu
                    420                 425                 430

tct cgg atg gag cgg gtg gtc cgc gaa cga atg tcc atc caa gac att        1344
Ser Arg Met Glu Arg Val Val Arg Glu Arg Met Ser Ile Gln Asp Ile
                435                 440                 445

tct agc acc aca ccc caa caa tta att aac atc cgt ccc gtt gta gct        1392
Ser Ser Thr Thr Pro Gln Gln Leu Ile Asn Ile Arg Pro Val Val Ala
            450                 455                 460

tct ctg aaa gaa ttt ttc ggg tct tcc caa ctc tcc caa ttc atg gac        1440
Ser Leu Lys Glu Phe Phe Gly Ser Ser Gln Leu Ser Gln Phe Met Asp
    465                 470                 475

caa acc aac ccc ttg ggt gag tta acc cac aaa cgt cgc ttg tct gcc        1488
Gln Thr Asn Pro Leu Gly Glu Leu Thr His Lys Arg Arg Leu Ser Ala
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     480                   485                   490                   495

ctt gga cca gga ggc ttg act agg gac cgg gct ggt tat gaa gtc cga    1536
Leu Gly Pro Gly Gly Leu Thr Arg Asp Arg Ala Gly Tyr Glu Val Arg
                500                   505                   510

gac gtc cac tat tcc cac tac ggc cgg atg tgc ccg atc gaa aca cct    1584
Asp Val His Tyr Ser His Tyr Gly Arg Met Cys Pro Ile Glu Thr Pro
                515                   520                   525

gaa ggc cca aac att ggt ctg att aac agt ttg tct acc tat gct aag    1632
Glu Gly Pro Asn Ile Gly Leu Ile Asn Ser Leu Ser Thr Tyr Ala Lys
                530                   535                   540

atc aat aaa ttt ggt ttt att gaa aca cct tac cgc cgg gtg gac cgg    1680
Ile Asn Lys Phe Gly Phe Ile Glu Thr Pro Tyr Arg Arg Val Asp Arg
            545                   550                   555

gaa act ggc cag gta acg gat aaa att gac tac ttg act gct gac gaa    1728
Glu Thr Gly Gln Val Thr Asp Lys Ile Asp Tyr Leu Thr Ala Asp Glu
560                   565                   570                   575

gaa gat ctt tac gtt gta gcc caa gcc aat gct gaa tta gat gaa gat    1776
Glu Asp Leu Tyr Val Val Ala Gln Ala Asn Ala Glu Leu Asp Glu Asp
                580                   585                   590

gga cat ttt gct aat gat gtc gtc cta gcc cga aga cgg gat gtc aac    1824
Gly His Phe Ala Asn Asp Val Val Leu Ala Arg Arg Arg Asp Val Asn
                595                   600                   605

gaa gag gtt gac gct tcc gaa gtt gac tat atg gac gtg tca cca aaa    1872
Glu Glu Val Asp Ala Ser Glu Val Asp Tyr Met Asp Val Ser Pro Lys
                610                   615                   620

caa gtt gtt tct gtg gcc aca gct tcc att cct ttc tta gaa aac gac    1920
Gln Val Val Ser Val Ala Thr Ala Ser Ile Pro Phe Leu Glu Asn Asp
            625                   630                   635

gac tcc aac cgg gct cta atg ggg gct aac atg caa cgg caa gct gtt    1968
Asp Ser Asn Arg Ala Leu Met Gly Ala Asn Met Gln Arg Gln Ala Val
640                   645                   650                   655

cct ctt atg caa cca gag tcc cca cta gta gga act gga atc gaa cac    2016
Pro Leu Met Gln Pro Glu Ser Pro Leu Val Gly Thr Gly Ile Glu His
                660                   665                   670

att gca gcc cgt gac tct gga gct gcc gtt att gcc aag gct gac ggg    2064
Ile Ala Ala Arg Asp Ser Gly Ala Ala Val Ile Ala Lys Ala Asp Gly
                675                   680                   685

gtt gtg gag tat gtt gat gcc aag acg gtc aaa gtc cgt caa gcc gat    2112
Val Val Glu Tyr Val Asp Ala Lys Thr Val Lys Val Arg Gln Ala Asp
                690                   695                   700

ggt acc ctc aac aac tac aag ctg gct aag tac aaa cgg tcc aac tcc    2160
Gly Thr Leu Asn Asn Tyr Lys Leu Ala Lys Tyr Lys Arg Ser Asn Ser
705                   710                   715
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gga act tct tac aac caa aga cca att gta aaa act ggt gag gaa gtt       2208
Gly Thr Ser Tyr Asn Gln Arg Pro Ile Val Lys Thr Gly Glu Glu Val
720                 725                 730                 735

gac aaa ggc gac atc cta gca gat ggt ccg tcc atg gaa aat ggt gaa       2256
Asp Lys Gly Asp Ile Leu Ala Asp Gly Pro Ser Met Glu Asn Gly Glu
                    740                 745                 750

atg gcc ctt ggt aaa aac cca ttg att gcc ttt acc acc ttt gat ggc       2304
Met Ala Leu Gly Lys Asn Pro Leu Ile Ala Phe Thr Thr Phe Asp Gly
                755                 760                 765

tac aac ttc gag gat gcc gtc att atg agt gaa cgt ttg gtc aaa gat       2352
Tyr Asn Phe Glu Asp Ala Val Ile Met Ser Glu Arg Leu Val Lys Asp
            770                 775                 780

gac gtt tat acc tcc atc cac att gaa gaa tat gaa tct gaa gcc cgc       2400
Asp Val Tyr Thr Ser Ile His Ile Glu Glu Tyr Glu Ser Glu Ala Arg
    785                 790                 795

gat acc aag tta ggg cca gaa gaa atc acc cgg gaa att cca aac gtc       2448
Asp Thr Lys Leu Gly Pro Glu Glu Ile Thr Arg Glu Ile Pro Asn Val
800                 805                 810                 815

ggg gaa agt gcc ctc aag aac ttg gat gaa aga ggc att atc cgg atc       2496
Gly Glu Ser Ala Leu Lys Asn Leu Asp Glu Arg Gly Ile Ile Arg Ile
                820                 825                 830

ggg gct gaa gtt cgt gac ggg gac atc cta gtt ggt aaa gtt aca ccc       2544
Gly Ala Glu Val Arg Asp Gly Asp Ile Leu Val Gly Lys Val Thr Pro
                835                 840                 845

aaa ggg gtt agt gaa cta tca gct gag gaa aaa ctc ctc cac gct atc       2592
Lys Gly Val Ser Glu Leu Ser Ala Glu Glu Lys Leu Leu His Ala Ile
                850                 855                 860

ttc ggc gaa aaa gcc cgg gaa gtt cgt gac acc tcc ctc cgt gtc cca       2640
Phe Gly Glu Lys Ala Arg Glu Val Arg Asp Thr Ser Leu Arg Val Pro
                865                 870                 875

cac ggt agt ggc gga att gtc cac gat gtc cag atc ttt acc cgg gaa       2688
His Gly Ser Gly Gly Ile Val His Asp Val Gln Ile Phe Thr Arg Glu
880                 885                 890                 895

gcc ggc gac gaa ctg tca cca ggc gtt aac tac ctt gtc cga gtt ttc       2736
Ala Gly Asp Glu Leu Ser Pro Gly Val Asn Tyr Leu Val Arg Val Phe
                900                 905                 910

att gcc caa aaa cgt aaa att gac gtt ggg gac aag atg gca ggt cga       2784
Ile Ala Gln Lys Arg Lys Ile Asp Val Gly Asp Lys Met Ala Gly Arg
                915                 920                 925

cac ggg aac aag ggt gtt gtt tcc ctt atc tta cca gaa gaa gac atg       2832
His Gly Asn Lys Gly Val Val Ser Leu Ile Leu Pro Glu Glu Asp Met
                930                 935                 940
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ccg ttt atg cca gac gga acc cca att gac atc atg ctc aac cca ctt    2880
Pro Phe Met Pro Asp Gly Thr Pro Ile Asp Ile Met Leu Asn Pro Leu
    945                 950             955

ggt gtc cct tcc cgg atg aat gtc ggc cag gtc atc gaa ctc cac atg    2928
Gly Val Pro Ser Arg Met Asn Val Gly Gln Val Ile Glu Leu His Met
960             965             970             975

ggg atg gca gcc cga cag tta ggc gag cac att gct act cca gtc ttt    2976
Gly Met Ala Ala Arg Gln Leu Gly Glu His Ile Ala Thr Pro Val Phe
            980             985             990

gac ggg gcc aac gaa gaa gat gtt tgg gaa act atc aag gaa gcc ggt    3024
Asp Gly Ala Asn Glu Glu Asp Val Trp Glu Thr Ile Lys Glu Ala Gly
            995             1000            1005

atg gat gca gat gcc aaa acc gtc ttg tat gac ggc cgg act ggc gag    3072
Met Asp Ala Asp Ala Lys Thr Val Leu Tyr Asp Gly Arg Thr Gly Glu
        1010            1015            1020

cca ttt gac aac aag gtc tcc gtt ggg gtg atg tac ttt atc aaa cta    3120
Pro Phe Asp Asn Lys Val Ser Val Gly Val Met Tyr Phe Ile Lys Leu
    1025            1030            1035

gtc cac atg gtc gac gac aag ttg cac gcc aga tcc aca gga cca tac    3168
Val His Met Val Asp Asp Lys Leu His Ala Arg Ser Thr Gly Pro Tyr
1040            1045            1050            1055

tcc ttg gtt acc caa caa ccc ctt ggt ggg aaa gca cag ttt ggt ggc    3216
Ser Leu Val Thr Gln Gln Pro Leu Gly Gly Lys Ala Gln Phe Gly Gly
            1060            1065            1070

caa cgc ttt ggt gag atg gaa gtc tgg gcc ttg gaa gct tat ggg gct    3264
Gln Arg Phe Gly Glu Met Glu Val Trp Ala Leu Glu Ala Tyr Gly Ala
            1075            1080            1085

tcc cgc acc ctc caa gaa atc ttg acc tac aag tca gat gac gtg att    3312
Ser Arg Thr Leu Gln Glu Ile Leu Thr Tyr Lys Ser Asp Asp Val Ile
        1090            1095            1100

gga agg gta gac acc tat gaa gcc att gtc aag ggc caa cgc att cca    3360
Gly Arg Val Asp Thr Tyr Glu Ala Ile Val Lys Gly Gln Arg Ile Pro
    1105            1110            1115

aaa cct ggt gta cct gaa tcc ttc cgt gtc ctc gtg aaa gaa ctc cag    3408
Lys Pro Gly Val Pro Glu Ser Phe Arg Val Leu Val Lys Glu Leu Gln
1120            1125            1130            1135

tct ctg ggg ttg gac ctg aaa gtc ctc gac aag gaa caa aac gaa atc    3456
Ser Leu Gly Leu Asp Leu Lys Val Leu Asp Lys Glu Gln Asn Glu Ile
            1140            1145            1150

aat ctc aag gct gaa gat gac gag tcg gaa gac caa gtc gtt gat tcc    3504
Asn Leu Lys Ala Glu Asp Asp Glu Ser Glu Asp Gln Val Val Asp Ser
            1155            1160            1165

cta gaa gaa atg cgt aaa gag cag gaa gaa gaa cgc cgt aag gaa aaa    3552
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Leu Glu Glu Met Arg Lys Glu Gln Glu Glu Glu Arg Arg Lys Glu Lys
        1170   1175   1180

gaa aaa gaa gag cca agt act gag tcg taa   3582
Glu Lys Glu Glu Pro Ser Thr Glu Ser
        1185   1190

<210> 14
<211> 1192
<212> PRT
<213> Alloiococcus otitidis

<400> 14
Met Asn Lys Leu Val Gly Lys Lys Val Asn Phe Gly Lys His Arg Val
1   5   10   15

Arg Arg Ser Tyr Ser Arg Ile Asn Glu Val Leu Glu Leu Pro Asn Leu
            20   25   30

Ile Glu Ile Gln Thr Asp Ser Tyr Asp Trp Phe Leu Asp Glu Gly Leu
        35   40   45

Lys Glu Met Phe Ser Asp Ile Ser Pro Ile Asp Asp Phe Ser Gly Asn
    50   55   60

Leu Ser Leu Glu Phe Val Asp Tyr Lys Phe Tyr Glu Ser Lys Tyr Thr
65   70   75   80

Val Glu Glu Ala Arg Glu His Asp Ala Asn Tyr Ser Ala Pro Leu Tyr
                85   90   95

Val Lys Leu Arg Leu Ile Asn Lys Glu Thr Gly Glu Val Lys Glu Gln
            100   105   110

Glu Val Phe Phe Gly Asp Phe Pro Leu Met Thr Glu Gln Gly Thr Phe
            115   120   125

Ile Ile Asn Gly Ala Glu Arg Val Ile Val Ser Gln Leu Val Arg Ser
        130   135   140

Pro Gly Val Tyr Tyr Ser Pro Lys Val Glu Lys Asn Gly Arg Glu Gly
145   150   155   160

Phe Ser Thr Val Leu Ile Pro Asn Arg Gly Ala Trp Leu Glu Tyr Glu
                165   170   175

Thr Asp Thr Lys Gly Ile Ser Asn Val Arg Ile Asp Arg Thr Arg Lys
        180   185   190

Ile Pro Ile Thr Val Leu Leu Arg Ala Leu Gly Ile Gly Ser Asp Asp
        195   200   205

Glu Ile Ile Asp Leu Ile Gly Leu Asn Asp Ser Leu Glu Ala Thr Leu
210   215   220

Glu Lys Asp Val His Lys Ser Thr Ser Asp Ser Arg Val Glu Glu Ala
225   230   235   240

Leu Lys Asp Leu Tyr Glu Arg Leu Arg Pro Gly Glu Pro Lys Thr Ala
                245   250   255

Glu Ser Ser Arg Asn Leu Ile Asn Thr Arg Phe Phe Asp His Lys Arg
                260   265   270

Tyr Asp Leu Ala Tyr Val Gly Arg Tyr Lys Met Asn Lys Lys Leu Asp
        275   280   285

Leu Lys Thr Arg Leu Met Gly Thr Val Leu Ala Glu Asn Leu Val Asp
        290   295   300

Pro Glu Ala Gly Glu Val Leu Ala Glu Glu Gly Ser Glu Val Thr Arg
305   310   315   320

Ser Val Met Asp Lys Leu Gly Pro Tyr Leu Asp Gly Asp Met Asn Gln
                325   330   335

Val Thr Ile Asn Pro Ser Glu Glu Ala Val Ile Pro Glu Pro Ile Asp
                340   345   350

Leu Gln Ile Val Lys Val Tyr Ser Lys Glu Asp Pro Asp Arg Ile Val
        355   360   365

Asn Met Ile Gly Asn Gly His Pro Asp Lys Lys Ala Lys Trp Ile Thr
        370   375   380

Pro Ala Asp Met Ile Ala Ala Met Ser Tyr Phe Phe Asn Leu Gln Glu
385   390   395   400

Gly Ile Gly Asp Val Asp Asp Ile Asp His Leu Gly Asn Arg Arg Ile
            405   410   415

Arg Ser Val Gly Glu Leu Leu Gln Asn Gln Phe Arg Ile Gly Leu Ser
            420   425   430

Arg Met Glu Arg Val Val Arg Glu Arg Met Ser Ile Gln Asp Ile Ser
            435   440   445

Ser Thr Thr Pro Gln Gln Leu Ile Asn Ile Arg Pro Val Val Ala Ser
    450   455   460

Leu Lys Glu Phe Phe Gly Ser Ser Gln Leu Ser Gln Phe Met Asp Gln
465   470   475   480

Thr Asn Pro Leu Gly Glu Leu Thr His Lys Arg Arg Leu Ser Ala Leu
            485   490   495

Gly Pro Gly Gly Leu Thr Arg Asp Arg Ala Gly Tyr Glu Val Arg Asp
            500   505   510

Val His Tyr Ser His Tyr Gly Arg Met Cys Pro Ile Glu Thr Pro Glu
            515   520   525

Gly Pro Asn Ile Gly Leu Ile Asn Ser Leu Ser Thr Tyr Ala Lys Ile
    530   535   540

Asn Lys Phe Gly Phe Ile Glu Thr Pro Tyr Arg Arg Val Asp Arg Glu
545   550   555   560

Thr Gly Gln Val Thr Asp Lys Ile Asp Tyr Leu Thr Ala Asp Glu Glu
            565   570   575

Asp Leu Tyr Val Val Ala Gln Ala Asn Ala Glu Leu Asp Glu Asp Gly
            580   585   590

His Phe Ala Asn Asp Val Val Leu Ala Arg Arg Arg Asp Val Asn Glu
    595   600   605

Glu Val Asp Ala Ser Glu Val Asp Tyr Met Asp Val Ser Pro Lys Gln
    610   615   620

Val Val Ser Val Ala Thr Ala Ser Ile Pro Phe Leu Glu Asn Asp Asp

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        625                   630                   635                   640

Ser Asn Arg Ala Leu Met Gly Ala Asn Met Gln Arg Gln Ala Val Pro
            645             650                 655

Leu Met Gln Pro Glu Ser Pro Leu Val Gly Thr Gly Ile Glu His Ile
            660         .       665                 670

Ala Ala Arg Asp Ser Gly Ala Ala Val Ile Ala Lys Ala Asp Gly Val
            675             680                 685

Val Glu Tyr Val Asp Ala Lys Thr Val Lys Val Arg Gln Ala Asp Gly
    690             695                 700

Thr Leu Asn Asn Tyr Lys Leu Ala Lys Tyr Lys Arg Ser Asn Ser Gly
 705                710                 715                 720

Thr Ser Tyr Asn Gln Arg Pro Ile Val Lys Thr Gly Glu Glu Val Asp
                725                 730                 735

Lys Gly Asp Ile Leu Ala Asp Gly Pro Ser Met Glu Asn Gly Glu Met
            740                 745                 750

Ala Leu Gly Lys Asn Pro Leu Ile Ala Phe Thr Thr Phe Asp Gly Tyr
            755                 760                 765

Asn Phe Glu Asp Ala Val Ile Met Ser Glu Arg Leu Val Lys Asp Asp
    770                 775                 780

Val Tyr Thr Ser Ile His Ile Glu Glu Tyr Glu Ser Glu Ala Arg Asp
785                 790                 795                 800

Thr Lys Leu Gly Pro Glu Glu Ile Thr Arg Glu Ile Pro Asn Val Gly
                805                 810                 815

Glu Ser Ala Leu Lys Asn Leu Asp Glu Arg Gly Ile Ile Arg Ile Gly
            820                 825                 830

Ala Glu Val Arg Asp Gly Asp Ile Leu Val Gly Lys Val Thr Pro Lys
            835                 840                 845

Gly Val Ser Glu Leu Ser Ala Glu Glu Lys Leu Leu His Ala Ile Phe
    850                 855                 860
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Gly Glu Lys Ala Arg Glu Val Arg Asp Thr Ser Leu Arg Val Pro His
865   870   875   880

Gly Ser Gly Gly Ile Val His Asp Val Gln Ile Phe Thr Arg Glu Ala
             885   890   895

Gly Asp Glu Leu Ser Pro Gly Val Asn Tyr Leu Val Arg Val Phe Ile
         900   905   910

Ala Gln Lys Arg Lys Ile Asp Val Gly Asp Lys Met Ala Gly Arg His
         915   920   925

Gly Asn Lys Gly Val Val Ser Leu Ile Leu Pro Glu Glu Asp Met Pro
     930   935   940

Phe Met Pro Asp Gly Thr Pro Ile Asp Ile Met Leu Asn Pro Leu Gly
945   950   955   960

Val Pro Ser Arg Met Asn Val Gly Gln Val Ile Glu Leu His Met Gly
             965   970   975

Met Ala Ala Arg Gln Leu Gly Glu His Ile Ala Thr Pro Val Phe Asp
         980   985   990

Gly Ala Asn Glu Glu Asp Val Trp Glu Thr Ile Lys Glu Ala Gly Met
     995   1000   1005

Asp Ala Asp Ala Lys Thr Val Leu Tyr Asp Gly Arg Thr Gly Glu Pro
     1010   1015   1020

Phe Asp Asn Lys Val Ser Val Gly Val Met Tyr Phe Ile Lys Leu Val
1025   1030   1035   1040

His Met Val Asp Asp Lys Leu His Ala Arg Ser Thr Gly Pro Tyr Ser
             1045   1050   1055

Leu Val Thr Gln Gln Pro Leu Gly Gly Lys Ala Gln Phe Gly Gly Gln
         1060   1065   1070

Arg Phe Gly Glu Met Glu Val Trp Ala Leu Glu Ala Tyr Gly Ala Ser
     1075   1080   1085

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Arg Thr Leu Gln Glu Ile Leu Thr Tyr Lys Ser Asp Asp Val Ile Gly
    1090            1095            1100

Arg Val Asp Thr Tyr Glu Ala Ile Val Lys Gly Gln Arg Ile Pro Lys
1105             1110            1115            1120

Pro Gly Val Pro Glu Ser Phe Arg Val Leu Val Lys Glu Leu Gln Ser
            1125            1130            1135

Leu Gly Leu Asp Leu Lys Val Leu Asp Lys Glu Gln Asn Glu Ile Asn
            1140            1145            1150

Leu Lys Ala Glu Asp Asp Glu Ser Glu Asp Gln Val Val Asp Ser Leu
    1155            1160            1165

Glu Glu Met Arg Lys Glu Gln Glu Glu Arg Arg Lys Glu Lys Glu
    1170            1175            1180

Lys Glu Glu Pro Ser Thr Glu Ser
1185            1190
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<210> 15
<211> 1407
<212> DNA
<213> Alloiococcus otitidis

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aaagaccagg aaaggaagaa gacc ttg gca act aat att cat gaa gac cgc        51
                          Met Ala Thr Asn Ile His Glu Asp Arg
                          1               5

ctg cca cca caa aat att gaa gcg gag caa tcc gtc tta ggg tcc gtc        99
Leu Pro Pro Gln Asn Ile Glu Ala Glu Gln Ser Val Leu Gly Ser Val
10              15              20              25

ctc tta aat gca gaa gcc ttg gtg gcg gcc atg gaa tat gtg gat gaa       147
Leu Leu Asn Ala Glu Ala Leu Val Ala Ala Met Glu Tyr Val Asp Glu
            30              35              40

gat gac ttt tac cgg cgg gcc cac cag ttg atc ttt aag gcc atg ata       195
Asp Asp Phe Tyr Arg Arg Ala His Gln Leu Ile Phe Lys Ala Met Ile
            45              50              55

gac ctc tat gaa gac aac cag gcc att gat gtc att acc att aaa gac       243
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        Asp Leu Tyr Glu Asp Asn Gln Ala Ile Asp Val Ile Thr Ile Lys Asp
                 60                  65                  70

aag ctg gaa gcc aat gac cag ttg gag gat atc ggg ggt gcc tct tac       291
Lys Leu Glu Ala Asn Asp Gln Leu Glu Asp Ile Gly Gly Ala Ser Tyr
         75                  80                  85

cta gct gag att gct ggg gtc acc cca acc gca gct aac gtg tcc tat       339
Leu Ala Glu Ile Ala Gly Val Thr Pro Thr Ala Ala Asn Val Ser Tyr
90                  95                  100                 105

tac gct aag att gtg gaa gat cgg tct ctt ttg cgc aac ttg att gcg       387
Tyr Ala Lys Ile Val Glu Asp Arg Ser Leu Leu Arg Asn Leu Ile Ala
                 110                 115                 120

aca gct aat gag att gcc cag tct ggc tac gaa gac cat gac gat gtg       435
Thr Ala Asn Glu Ile Ala Gln Ser Gly Tyr Glu Asp His Asp Asp Val
                 125                 130                 135

cca gaa gtt tta aac aat gct gag cag aag atc ttg cag gtt tct gaa       483
Pro Glu Val Leu Asn Asn Ala Glu Gln Lys Ile Leu Gln Val Ser Glu
                 140                 145                 150

aaa cga aac cgg acc ggc ttt gct agt att tca gaa atc ctc cac caa       531
Lys Arg Asn Arg Thr Gly Phe Ala Ser Ile Ser Glu Ile Leu His Gln
         155                 160                 165

acc atc gag cat att gat gaa ctc cac caa agg gat gaa gag atc acc       579
Thr Ile Glu His Ile Asp Glu Leu His Gln Arg Asp Glu Glu Ile Thr
170                 175                 180                 185

ggg att tca act ggc tac ccc tac ctg gac agg atg act tca ggc ctt       627
Gly Ile Ser Thr Gly Tyr Pro Tyr Leu Asp Arg Met Thr Ser Gly Leu
                 190                 195                 200

cat gaa gat gag ttg att att gtc gca gca aga ccg ggt gtg ggg aaa       675
His Glu Asp Glu Leu Ile Ile Val Ala Ala Arg Pro Gly Val Gly Lys
                 205                 210                 215

acg gct ttt gcc ttg aat gtc gcc caa aat atc ggg aca gcc aca gat       723
Thr Ala Phe Ala Leu Asn Val Ala Gln Asn Ile Gly Thr Ala Thr Asp
         220                 225                 230

gaa act att gcg att ttt tcc ctt gag atg ggg gct gaa cag ctg gtc       771
Glu Thr Ile Ala Ile Phe Ser Leu Glu Met Gly Ala Glu Gln Leu Val
         235                 240                 245

aac cgg atg tta tgt tca gaa ggc agt att gat gcc act aac ctc cga       819
Asn Arg Met Leu Cys Ser Glu Gly Ser Ile Asp Ala Thr Asn Leu Arg
250                 255                 260                 265

aat ggc aag cta acg ccg gaa gaa tat gac cgt ttg ttt gtg gcc atg       867
Asn Gly Lys Leu Thr Pro Glu Glu Tyr Asp Arg Leu Phe Val Ala Met
                 270                 275                 280

ggg agc ttg tct gaa gct gat att tat att gat gac act ccc ggc atc       915
Gly Ser Leu Ser Glu Ala Asp Ile Tyr Ile Asp Asp Thr Pro Gly Ile
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              285                 290                 295

cgg aca gct gaa atc cgg gcc aag tgc cgc cgc ctg gtc caa gag aag      963
Arg Thr Ala Glu Ile Arg Ala Lys Cys Arg Arg Leu Val Gln Glu Lys
        300                 305                 310

gga agt ctg ggc ttg att gtc att gac tac ctg caa ttg atc gaa gga    1011
Gly Ser Leu Gly Leu Ile Val Ile Asp Tyr Leu Gln Leu Ile Glu Gly
        315                 320                 325

gct tca aac tat gaa tcc aga cag cag cag gtg tct gat ata tct cgg    1059
Ala Ser Asn Tyr Glu Ser Arg Gln Gln Gln Val Ser Asp Ile Ser Arg
330                 335                 340                 345

cag ctg aag aag ctt tct aag gaa ctt tct gtc cca gtt att gcc ctg    1107
Gln Leu Lys Lys Leu Ser Lys Glu Leu Ser Val Pro Val Ile Ala Leu
                350                 355                 360

tca caa ctg tcc cgg agt gtg gaa cag aga caa gac aag cgg ccc atc    1155
Ser Gln Leu Ser Arg Ser Val Glu Gln Arg Gln Asp Lys Arg Pro Ile
                365                 370                 375

ctc agt gac ttg cgg gaa tca ggg tcg att gaa cag gat gcc gat att    1203
Leu Ser Asp Leu Arg Glu Ser Gly Ser Ile Glu Gln Asp Ala Asp Ile
                380                 385                 390

gtg gcc ttc ctt tac cgg gag gac tac tac caa aat gaa gaa gat atc    1251
Val Ala Phe Leu Tyr Arg Glu Asp Tyr Tyr Gln Asn Glu Glu Asp Ile
        395                 400                 405

gat gag gac ttt gtc gat aat agc gtg gaa gtc att atc gaa aaa aac    1299
Asp Glu Asp Phe Val Asp Asn Ser Val Glu Val Ile Ile Glu Lys Asn
410                 415                 420                 425

cgg tca gga gct cga gga aca gtc aag ttg aac ttt aag aaa gag ttc    1347
Arg Ser Gly Ala Arg Gly Thr Val Lys Leu Asn Phe Lys Lys Glu Phe
                430                 435                 440

aac aaa ttt acc tcg att tct tac cgg tct gaa gat gaa gtc cca gcc    1395
Asn Lys Phe Thr Ser Ile Ser Tyr Arg Ser Glu Asp Glu Val Pro Ala
                445                 450                 455

aac ttt ggc tag                                                    1407
Asn Phe Gly
        460


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<212> PRT
<213> Alloiococcus otitidis

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1               5                   10                  15
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Ala Glu Gln Ser Val Leu Gly Ser Val Leu Leu Asn Ala Glu Ala Leu
        20   25   30

Val Ala Ala Met Glu Tyr Val Asp Glu Asp Asp Phe Tyr Arg Arg Ala
        35   40   45

His Gln Leu Ile Phe Lys Ala Met Ile Asp Leu Tyr Glu Asp Asn Gln
    50   55   60

Ala Ile Asp Val Ile Thr Ile Lys Asp Lys Leu Glu Ala Asn Asp Gln
65   70   75   80

Leu Glu Asp Ile Gly Gly Ala Ser Tyr Leu Ala Glu Ile Ala Gly Val
            85   90   95

Thr Pro Thr Ala Ala Asn Val Ser Tyr Tyr Ala Lys Ile Val Glu Asp
            100   105   110

Arg Ser Leu Leu Arg Asn Leu Ile Ala Thr Ala Asn Glu Ile Ala Gln
        115   120   125

Ser Gly Tyr Glu Asp His Asp Asp Val Pro Glu Val Leu Asn Asn Ala
        130   135   140

Glu Gln Lys Ile Leu Gln Val Ser Glu Lys Arg Asn Arg Thr Gly Phe
145   150   155   160

Ala Ser Ile Ser Glu Ile Leu His Gln Thr Ile Glu His Ile Asp Glu
            165   170   175

Leu His Gln Arg Asp Glu Glu Ile Thr Gly Ile Ser Thr Gly Tyr Pro
        180   185   190

Tyr Leu Asp Arg Met Thr Ser Gly Leu His Glu Asp Glu Leu Ile Ile
        195   200   205

Val Ala Ala Arg Pro Gly Val Gly Lys Thr Ala Phe Ala Leu Asn Val
    210   215   220

Ala Gln Asn Ile Gly Thr Ala Thr Asp Glu Thr Ile Ala Ile Phe Ser
225   230   235   240

Leu Glu Met Gly Ala Glu Gln Leu Val Asn Arg Met Leu Cys Ser Glu

                    245   250   255

Gly Ser Ile Asp Ala Thr Asn Leu Arg Asn Gly Lys Leu Thr Pro Glu
              260   265   270

Glu Tyr Asp Arg Leu Phe Val Ala Met Gly Ser Leu Ser Glu Ala Asp
              275   280   285

Ile Tyr Ile Asp Asp Thr Pro Gly Ile Arg Thr Ala Glu Ile Arg Ala
      290   295   300

Lys Cys Arg Arg Leu Val Gln Glu Lys Gly Ser Leu Gly Leu Ile Val
305   310   315   320

Ile Asp Tyr Leu Gln Leu Ile Glu Gly Ala Ser Asn Tyr Glu Ser Arg
                  325   330   335

Gln Gln Gln Val Ser Asp Ile Ser Arg Gln Leu Lys Lys Leu Ser Lys
              340   345   350

Glu Leu Ser Val Pro Val Ile Ala Leu Ser Gln Leu Ser Arg Ser Val
       355   360   365

Glu Gln Arg Gln Asp Lys Arg Pro Ile Leu Ser Asp Leu Arg Glu Ser
       370   375   380

Gly Ser Ile Glu Gln Asp Ala Asp Ile Val Ala Phe Leu Tyr Arg Glu
385   390   395   400

Asp Tyr Tyr Gln Asn Glu Glu Asp Ile Asp Glu Asp Phe Val Asp Asn
              405   410   415

Ser Val Glu Val Ile Ile Glu Lys Asn Arg Ser Gly Ala Arg Gly Thr
              420   425   430

Val Lys Leu Asn Phe Lys Lys Glu Phe Asn Lys Phe Thr Ser Ile Ser
       435   440   445

Tyr Arg Ser Glu Asp Glu Val Pro Ala Asn Phe Gly
    450   455   460

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<212> DNA
<213> Alloiococcus otitidis

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          Met Phe Leu Glu Glu Arg Asp Ser Arg Leu Glu Gln Ile Lys
          1            5                    10

ctg tcc aag gag atg aaa aac tca ttc tta gac tat gcc atg agt gtc          99
Leu Ser Lys Glu Met Lys Asn Ser Phe Leu Asp Tyr Ala Met Ser Val
15              20              25                  30

atc gtc tcc cgg gcc cta ccc gat gtc cgg gac ggc ttg aag ccg gtt        147
Ile Val Ser Arg Ala Leu Pro Asp Val Arg Asp Gly Leu Lys Pro Val
                35              40                  45

cac cga aga atc ctg tac gga atg aat gaa ctg ggc tta acc ccg gac        195
His Arg Arg Ile Leu Tyr Gly Met Asn Glu Leu Gly Leu Thr Pro Asp
            50              55              60

aag tct tat aaa aag tct gcc cgt att gta ggg gat gtt atg ggg aaa        243
Lys Ser Tyr Lys Lys Ser Ala Arg Ile Val Gly Asp Val Met Gly Lys
            65              70              75

tac cac ccc cac ggt gac act gct att tat gac tcc atg gtc aga atg        291
Tyr His Pro His Gly Asp Thr Ala Ile Tyr Asp Ser Met Val Arg Met
        80              85              90

gcc cag gac ttt tct tac cga gtt ccc tta gtg gac ggc cat ggg aac        339
Ala Gln Asp Phe Ser Tyr Arg Val Pro Leu Val Asp Gly His Gly Asn
95              100             105                 110

ttt ggg tcg gtt gac ggg gac gga gct gct gcc atg cgg tat acc gaa        387
Phe Gly Ser Val Asp Gly Asp Gly Ala Ala Ala Met Arg Tyr Thr Glu
                115             120             125

gcc cgg atg tcc aag atg gcc ttg gaa ctc ctg cga gac atc aac aag        435
Ala Arg Met Ser Lys Met Ala Leu Glu Leu Leu Arg Asp Ile Asn Lys
            130             135             140

gat acc att gac tac cac gat aac tat gat ggg act gag tcg gaa ccc        483
Asp Thr Ile Asp Tyr His Asp Asn Tyr Asp Gly Thr Glu Ser Glu Pro
            145             150             155

gat atc ctt cct gcc cgc ttc ccc aac ctc tta gtc aac ggg gct tcg        531
Asp Ile Leu Pro Ala Arg Phe Pro Asn Leu Leu Val Asn Gly Ala Ser
        160             165             170

ggg att gct gtt ggg atg gca acc aat atc cca ccc cac aat ctt aag        579
Gly Ile Ala Val Gly Met Ala Thr Asn Ile Pro Pro His Asn Leu Lys
175             180             185             190
```

```
gaa gtc att gat gcc tgc gtc ctc ttg atg gaa aat gag gat gtg act      627
Glu Val Ile Asp Ala Cys Val Leu Leu Met Glu Asn Glu Asp Val Thr
            195                 200                 205

gtg gct gac ctt atg gaa gtc tta cca gga cct gac ttt ccg act ggg      675
Val Ala Asp Leu Met Glu Val Leu Pro Gly Pro Asp Phe Pro Thr Gly
            210                 215                 220

gct tcc ctt att ggt gtt tct ggc gtc cgc aag gct tat gag acc ggt      723
Ala Ser Leu Ile Gly Val Ser Gly Val Arg Lys Ala Tyr Glu Thr Gly
            225                 230                 235

cgt ggg tcc att aaa tta cgg gcc aag tcc cgg atc gat gtc gac caa      771
Arg Gly Ser Ile Lys Leu Arg Ala Lys Ser Arg Ile Asp Val Asp Gln
        240                 245                 250

aaa ggt aag gaa aga att att atc gac gaa att cct tac atg gtc aac      819
Lys Gly Lys Glu Arg Ile Ile Ile Asp Glu Ile Pro Tyr Met Val Asn
255                 260                 265                 270

aag gcc aaa ttg gtc gaa aag att gcg gaa ctg gct cgg gac aag aaa      867
Lys Ala Lys Leu Val Glu Lys Ile Ala Glu Leu Ala Arg Asp Lys Lys
            275                 280                 285

att gac ggc att acc gat tta aat gat gag tct gac cgg gaa ggc ttg      915
Ile Asp Gly Ile Thr Asp Leu Asn Asp Glu Ser Asp Arg Glu Gly Leu
            290                 295                 300

cgg att gtg atc gat gta cgc cgg gat act tct gct ggt ata tta ctt      963
Arg Ile Val Ile Asp Val Arg Arg Asp Thr Ser Ala Gly Ile Leu Leu
            305                 310                 315

aac aag ctt tac aaa atg acc caa ttg cag gtt tct ttt ggc ttt aac     1011
Asn Lys Leu Tyr Lys Met Thr Gln Leu Gln Val Ser Phe Gly Phe Asn
            320                 325                 330

atg ctg gct atc gtc gat ggg gtg ccc aaa acc ttg ggc ctc aaa gac     1059
Met Leu Ala Ile Val Asp Gly Val Pro Lys Thr Leu Gly Leu Lys Asp
335                 340                 345                 350

atc ctg acc cac tac tta gac cat caa aaa act gtt atc cgc agg cgg     1107
Ile Leu Thr His Tyr Leu Asp His Gln Lys Thr Val Ile Arg Arg Arg
            355                 360                 365

aca gag ttt gac aag aac aag gct gaa tcg cgg gcc cac atc tta gaa     1155
Thr Glu Phe Asp Lys Asn Lys Ala Glu Ser Arg Ala His Ile Leu Glu
            370                 375                 380

ggg ctt cgg act gcc tta gac cat atc gat gcc att att acc att atc     1203
Gly Leu Arg Thr Ala Leu Asp His Ile Asp Ala Ile Ile Thr Ile Ile
            385                 390                 395

cgt cag tcc cag caa gct gaa gaa gcc aaa agt caa ttg atg gct tct     1251
Arg Gln Ser Gln Gln Ala Glu Glu Ala Lys Ser Gln Leu Met Ala Ser
            400                 405                 410

tat gac ctc tct gac cgt caa gcc cag gcg att tta gac atg cgg atg     1299
```

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Tyr Asp Leu Ser Asp Arg Gln Ala Gln Ala Ile Leu Asp Met Arg Met
415             420             425             430

gtc cgg ttg act ggt ttg gaa aga gag aaa att gaa gat gaa tac gct    1347
Val Arg Leu Thr Gly Leu Glu Arg Glu Lys Ile Glu Asp Glu Tyr Ala
                435             440             445

gaa ctc tta gaa aaa atc gag gac ttg cgt gac atc ttg gcc cgg cca    1395
Glu Leu Leu Glu Lys Ile Glu Asp Leu Arg Asp Ile Leu Ala Arg Pro
                450             455             460

gaa cgg atc aag caa att atc aaa gaa gaa atg atc gaa att gct gaa    1443
Glu Arg Ile Lys Gln Ile Ile Lys Glu Glu Met Ile Glu Ile Ala Glu
            465             470             475

aaa cac ggc caa gac cgc cta act gac atc cgg gtt ggg gaa gag ttg    1491
Lys His Gly Gln Asp Arg Leu Thr Asp Ile Arg Val Gly Glu Glu Leu
            480             485             490

agc att gaa gac gaa gac ttg att gaa gaa gaa gat atc atc att acc    1539
Ser Ile Glu Asp Glu Asp Leu Ile Glu Glu Glu Asp Ile Ile Ile Thr
495             500             505             510

ctg tct cga aaa ggc tat atc aaa cgg atg ccg gct gga gaa ttc aag    1587
Leu Ser Arg Lys Gly Tyr Ile Lys Arg Met Pro Ala Gly Glu Phe Lys
                515             520             525

gcc caa aac cgc ggt ggc cgt ggg gtt aag ggg atg act acc aac gat    1635
Ala Gln Asn Arg Gly Gly Arg Gly Val Lys Gly Met Thr Thr Asn Asp
                530             535             540

ggg gac ttt gtt gaa cag ctg act ttc tgt tct agt cat gac caa atc    1683
Gly Asp Phe Val Glu Gln Leu Thr Phe Cys Ser Ser His Asp Gln Ile
                545             550             555

ctc ttc ttt acc aac caa ggc aag gtt tat aag atc aag gcc tac gaa    1731
Leu Phe Phe Thr Asn Gln Gly Lys Val Tyr Lys Ile Lys Ala Tyr Glu
                560             565             570

atc ccg gaa tat ggg cgt aat gcc aag gga att cct gcc atc aac ttt    1779
Ile Pro Glu Tyr Gly Arg Asn Ala Lys Gly Ile Pro Ala Ile Asn Phe
575             580             585             590

tta aat ata gat aaa gat gaa tat att caa gcc atg gtc aac ttg act    1827
Leu Asn Ile Asp Lys Asp Glu Tyr Ile Gln Ala Met Val Asn Leu Thr
                595             600             605

gac cag gca gat gac cag gac caa ttc ttc ttt gcg aca aga ctt ggc    1875
Asp Gln Ala Asp Asp Gln Asp Gln Phe Phe Phe Ala Thr Arg Leu Gly
            610             615             620

cgg gtc aaa cgg acg gcc cag tct gaa ttt caa aat atc aga agt agc    1923
Arg Val Lys Arg Thr Ala Gln Ser Glu Phe Gln Asn Ile Arg Ser Ser
            625             630             635

ggg ttg aac gcg atc aat cta aat gaa ggc gat gaa ttg gtt aac gtg    1971
Gly Leu Asn Ala Ile Asn Leu Asn Glu Gly Asp Glu Leu Val Asn Val
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              640                   645                   650
    gtc cct acc cac aat gac cag gcc att atc ctg gcc agc cag caa ggc      2019
    Val Pro Thr His Asn Asp Gln Ala Ile Ile Leu Ala Ser Gln Gln Gly
    655                   660                   665                   670

    tat gcg gtc tac ttt gat gaa aaa gat atc cgt agc atg ggt cga ggg      2067
    Tyr Ala Val Tyr Phe Asp Glu Lys Asp Ile Arg Ser Met Gly Arg Gly
                          675                   680                   685

    gct gca ggt gtc cgt gga att cgc tta ggt gat ggc gac aca gtg gtt      2115
    Ala Ala Gly Val Arg Gly Ile Arg Leu Gly Asp Gly Asp Thr Val Val
                          690                   695                   700

    gcc atg gaa gtc tta gag ccg ggc caa gac gta tta gtc att act gaa      2163
    Ala Met Glu Val Leu Glu Pro Gly Gln Asp Val Leu Val Ile Thr Glu
                  705                   710                   715

    aaa ggg tac ggc aaa cga acc tcc caa gaa gag tac acc ctc cac aag      2211
    Lys Gly Tyr Gly Lys Arg Thr Ser Gln Glu Glu Tyr Thr Leu His Lys
                  720                   725                   730

    cga ggg ggc aag ggg gtt aaa acc ctt cat att acc gat aag aat ggt      2259
    Arg Gly Gly Lys Gly Val Lys Thr Leu His Ile Thr Asp Lys Asn Gly
    735                   740                   745                   750

    ccc cta att gga ctg aaa act gtc tct ggt ggt gag gac gtc atg att      2307
    Pro Leu Ile Gly Leu Lys Thr Val Ser Gly Gly Glu Asp Val Met Ile
                          755                   760                   765

    gtc acc gac caa ggt atc atg att cgt atc gaa gcc gac agc atc tct      2355
    Val Thr Asp Gln Gly Ile Met Ile Arg Ile Glu Ala Asp Ser Ile Ser
                          770                   775                   780

    cag acc tcc cgc cta acc caa ggt gtc cgt tta att cga ctt gaa gaa      2403
    Gln Thr Ser Arg Leu Thr Gln Gly Val Arg Leu Ile Arg Leu Glu Glu
                  785                   790                   795

    gat agc cgg gtg tca acg gta gcc ctc att gat att gac caa gag ctt      2451
    Asp Ser Arg Val Ser Thr Val Ala Leu Ile Asp Ile Asp Gln Glu Leu
                  800                   805                   810

    gac aat caa gtt aac caa acc gtt gag gaa taa                          2484
    Asp Asn Gln Val Asn Gln Thr Val Glu Glu
    815                   820


    <210> 18
    <211> 824
    <212> PRT
    <213> Alloiococcus otitidis

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    1                   5                   10                   15
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Lys Glu Met Lys Asn Ser Phe Leu Asp Tyr Ala Met Ser Val Ile Val
            20   25   30

Ser Arg Ala Leu Pro Asp Val Arg Asp Gly Leu Lys Pro Val His Arg
            35   40   45

Arg Ile Leu Tyr Gly Met Asn Glu Leu Gly Leu Thr Pro Asp Lys Ser
    50   55   60

Tyr Lys Lys Ser Ala Arg Ile Val Gly Asp Val Met Gly Lys Tyr His
65   70   75   80

Pro His Gly Asp Thr Ala Ile Tyr Asp Ser Met Val Arg Met Ala Gln
                85   90   95

Asp Phe Ser Tyr Arg Val Pro Leu Val Asp Gly His Gly Asn Phe Gly
            100   105   110

Ser Val Asp Gly Asp Gly Ala Ala Ala Met Arg Tyr Thr Glu Ala Arg
            115   120   125

Met Ser Lys Met Ala Leu Glu Leu Leu Arg Asp Ile Asn Lys Asp Thr
    130   135   140

Ile Asp Tyr His Asp Asn Tyr Asp Gly Thr Glu Ser Glu Pro Asp Ile
145   150   155   160

Leu Pro Ala Arg Phe Pro Asn Leu Leu Val Asn Gly Ala Ser Gly Ile
                165   170   175

Ala Val Gly Met Ala Thr Asn Ile Pro Pro His Asn Leu Lys Glu Val
            180   185   190

Ile Asp Ala Cys Val Leu Leu Met Glu Asn Glu Asp Val Thr Val Ala
        195   200   205

Asp Leu Met Glu Val Leu Pro Gly Pro Asp Phe Pro Thr Gly Ala Ser
    210   215   220

Leu Ile Gly Val Ser Gly Val Arg Lys Ala Tyr Glu Thr Gly Arg Gly
225   230   235   240

Ser Ile Lys Leu Arg Ala Lys Ser Arg Ile Asp Val Asp Gln Lys Gly

                    245   250   255

Lys Glu Arg Ile Ile Ile Asp Glu Ile Pro Tyr Met Val Asn Lys Ala
          260   265   270

Lys Leu Val Glu Lys Ile Ala Glu Leu Ala Arg Asp Lys Lys Ile Asp
          275   280   285

Gly Ile Thr Asp Leu Asn Asp Glu Ser Asp Arg Glu Gly Leu Arg Ile
          290   295   300

Val Ile Asp Val Arg Arg Asp Thr Ser Ala Gly Ile Leu Leu Asn Lys
305   310   315   320

Leu Tyr Lys Met Thr Gln Leu Gln Val Ser Phe Gly Phe Asn Met Leu
                    325   330   335

Ala Ile Val Asp Gly Val Pro Lys Thr Leu Gly Leu Lys Asp Ile Leu
          340   345   350

Thr His Tyr Leu Asp His Gln Lys Thr Val Ile Arg Arg Arg Thr Glu
          355   360   365

Phe Asp Lys Asn Lys Ala Glu Ser Arg Ala His Ile Leu Glu Gly Leu
          370   375   380

Arg Thr Ala Leu Asp His Ile Asp Ala Ile Ile Thr Ile Ile Arg Gln
385   390   395   400

Ser Gln Gln Ala Glu Glu Ala Lys Ser Gln Leu Met Ala Ser Tyr Asp
                    405   410   415

Leu Ser Asp Arg Gln Ala Gln Ala Ile Leu Asp Met Arg Met Val Arg
          420   425   430

Leu Thr Gly Leu Glu Arg Glu Lys Ile Glu Asp Glu Tyr Ala Glu Leu
          435   440   445

Leu Glu Lys Ile Glu Asp Leu Arg Asp Ile Leu Ala Arg Pro Glu Arg
          450   455   460

Ile Lys Gln Ile Ile Lys Glu Glu Met Ile Glu Ile Ala Glu Lys His
465   470   475   480

Gly Gln Asp Arg Leu Thr Asp Ile Arg Val Gly Glu Glu Leu Ser Ile
           485   490   495

Glu Asp Glu Asp Leu Ile Glu Glu Glu Asp Ile Ile Ile Thr Leu Ser
           500   505   510

Arg Lys Gly Tyr Ile Lys Arg Met Pro Ala Gly Glu Phe Lys Ala Gln
           515   520   525

Asn Arg Gly Gly Arg Gly Val Lys Gly Met Thr Thr Asn Asp Gly Asp
        530   535   540

Phe Val Glu Gln Leu Thr Phe Cys Ser Ser His Asp Gln Ile Leu Phe
545   550   555   560

Phe Thr Asn Gln Gly Lys Val Tyr Lys Ile Lys Ala Tyr Glu Ile Pro
           565   570   575

Glu Tyr Gly Arg Asn Ala Lys Gly Ile Pro Ala Ile Asn Phe Leu Asn
        580   585   590

Ile Asp Lys Asp Glu Tyr Ile Gln Ala Met Val Asn Leu Thr Asp Gln
       595   600   605

Ala Asp Asp Gln Asp Gln Phe Phe Phe Ala Thr Arg Leu Gly Arg Val
      610   615   620

Lys Arg Thr Ala Gln Ser Glu Phe Gln Asn Ile Arg Ser Ser Gly Leu
625   630   635   640

Asn Ala Ile Asn Leu Asn Glu Gly Asp Glu Leu Val Asn Val Val Pro
           575   650   655

Thr His Asn Asp Gln Ala Ile Ile Leu Ala Ser Gln Gln Gly Tyr Ala
          660   665   670

Val Tyr Phe Asp Glu Lys Asp Ile Arg Ser Met Gly Arg Gly Ala Ala
      675   680   685

Gly Val Arg Gly Ile Arg Leu Gly Asp Gly Asp Thr Val Val Ala Met
      690   695   700

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Glu Val Leu Glu Pro Gly Gln Asp Val Leu Val Ile Thr Glu Lys Gly
705               710               715               720


Tyr Gly Lys Arg Thr Ser Gln Glu Glu Tyr Thr Leu His Lys Arg Gly
                  725               730               735


Gly Lys Gly Val Lys Thr Leu His Ile Thr Asp Lys Asn Gly Pro Leu
              740               745               750


Ile Gly Leu Lys Thr Val Ser Gly Gly Glu Asp Val Met Ile Val Thr
          755               760               765


Asp Gln Gly Ile Met Ile Arg Ile Glu Ala Asp Ser Ile Ser Gln Thr
    770               775               780


Ser Arg Leu Thr Gln Gly Val Arg Leu Ile Arg Leu Glu Glu Asp Ser
785               790               795               800


Arg Val Ser Thr Val Ala Leu Ile Asp Ile Asp Gln Glu Leu Asp Asn
              805               810               815


Gln Val Asn Gln Thr Val Glu Glu
              820
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<210> 19
<211> 1956
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<213> Alloiococcus otitidis

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<221> CDS
<222> (7)..(1956)
<223>

<400> 19
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       Met Ala Glu Asp Arg Pro Leu Thr Pro Asn Glu Leu Ala Glu
       1           5                   10


ctg aaa aaa aca tat gat gct agt caa atc caa gtc tta gaa ggc cta       96
Leu Lys Lys Thr Tyr Asp Ala Ser Gln Ile Gln Val Leu Glu Gly Leu
15              20                  25                  30


gaa gca gtc aga gta cgg ccg ggt atg tac att ggg tcc acc agc aag      144
Glu Ala Val Arg Val Arg Pro Gly Met Tyr Ile Gly Ser Thr Ser Lys
                35                  40                  45


gaa ggc ctc cac cac ttg gta tgg gag atc gtg gac aat gct att gac      192
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        Glu Gly Leu His His Leu Val Trp Glu Ile Val Asp Asn Ala Ile Asp
                    50                  55                  60

        gaa gct atg gcc ggt tat gcc gac aag att tct gtt tcc att ttg gaa    240
        Glu Ala Met Ala Gly Tyr Ala Asp Lys Ile Ser Val Ser Ile Leu Glu
                    65                  70                  75

        ggc gac gtg atc caa gtg gct gat aac ggc cgg ggc atc ccg gtt gat    288
        Gly Asp Val Ile Gln Val Ala Asp Asn Gly Arg Gly Ile Pro Val Asp
                80                  85                  90

        atc cag gaa aaa aca ggc cgg cca gct gtt gaa act gtc ttt aca gtc    336
        Ile Gln Glu Lys Thr Gly Arg Pro Ala Val Glu Thr Val Phe Thr Val
        95                  100                 105                 110

        ctc cac gct ggt ggg aaa ttt ggt ggc ggt ggt tac aag gtt tcc ggt    384
        Leu His Ala Gly Gly Lys Phe Gly Gly Gly Gly Tyr Lys Val Ser Gly
                        115                 120                 125

        ggt ctg cac ggt gta ggg tct tct gtg gtc aat gct ctc tcc gaa tac    432
        Gly Leu His Gly Val Gly Ser Ser Val Val Asn Ala Leu Ser Glu Tyr
                        130                 135                 140

        ctc caa gtc cag gtg cac cga gat ggt aaa atc tac caa caa gtt tac    480
        Leu Gln Val Gln Val His Arg Asp Gly Lys Ile Tyr Gln Gln Val Tyr
                        145                 150                 155

        aag cgg ggc ttg gtt gat tct gac ttg gaa gtg gtg ggt gag act gac    528
        Lys Arg Gly Leu Val Asp Ser Asp Leu Glu Val Val Gly Glu Thr Asp
                    160                 165                 170

        cac act gga act att gtt acc ttt aag gca gat agt ttg att ttt aaa    576
        His Thr Gly Thr Ile Val Thr Phe Lys Ala Asp Ser Leu Ile Phe Lys
        175                 180                 185                 190

        gac act act tct tat gac ttc aat acc tta gcc acc cgg atc cgg gag    624
        Asp Thr Thr Ser Tyr Asp Phe Asn Thr Leu Ala Thr Arg Ile Arg Glu
                        195                 200                 205

        ttg gcc ttc tta aac cga ggc ttg aat att tcc atc gaa gac aaa cgg    672
        Leu Ala Phe Leu Asn Arg Gly Leu Asn Ile Ser Ile Glu Asp Lys Arg
                        210                 215                 220

        caa gca ggc ggg cag tct ttg aac tac cac tat gaa ggt ggg ata tcg    720
        Gln Ala Gly Gly Gln Ser Leu Asn Tyr His Tyr Glu Gly Gly Ile Ser
                    225                 230                 235

        agt tat gtt gac cac ttg aat tcc agc cgt gaa gtt ctt tat gag acc    768
        Ser Tyr Val Asp His Leu Asn Ser Ser Arg Glu Val Leu Tyr Glu Thr
                    240                 245                 250

        cca att ttc ttg gaa ggg gaa gaa gaa ggg att tct gtg gaa att gcc    816
        Pro Ile Phe Leu Glu Gly Glu Glu Glu Gly Ile Ser Val Glu Ile Ala
        255                 260                 265                 270

        ctc cag cat acc gat agc ttc cat act aat tta atg agt ttt gcc aat    864
        Leu Gln His Thr Asp Ser Phe His Thr Asn Leu Met Ser Phe Ala Asn
```

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             275              280              285

aac atc cac acc tat gag ggt ggc atg cat att tcc ggc ttc aag aca        912
Asn Ile His Thr Tyr Glu Gly Gly Met His Ile Ser Gly Phe Lys Thr
             290              295              300

gcc ctt acc cgg gcg gtc aac gac tat gcc cgg cag aat aac ttg ctc        960
Ala Leu Thr Arg Ala Val Asn Asp Tyr Ala Arg Gln Asn Asn Leu Leu
             305              310              315

cga gag tca gag gat aac ttt acc ggc gat gac gtt cgg gaa ggt ctg       1008
Arg Glu Ser Glu Asp Asn Phe Thr Gly Asp Asp Val Arg Glu Gly Leu
             320              325              330

acg gtg gtt ttg tca atc aag cac cca gac ccc caa ttt gaa gga caa       1056
Thr Val Val Leu Ser Ile Lys His Pro Asp Pro Gln Phe Glu Gly Gln
335              340              345              350

acc aag act aag ctg ggg aac tct gaa gtc aga ggg ata att gac cgg       1104
Thr Lys Thr Lys Leu Gly Asn Ser Glu Val Arg Gly Ile Ile Asp Arg
             355              360              365

ctc ttt agc cag cac ttt gaa cgt tac ctc atg gaa aat cca aag gtt       1152
Leu Phe Ser Gln His Phe Glu Arg Tyr Leu Met Glu Asn Pro Lys Val
             370              375              380

ggt aag cgg att gtt gac aag gcg ctt ttg gct tcc aaa gcc cgc caa       1200
Gly Lys Arg Ile Val Asp Lys Ala Leu Leu Ala Ser Lys Ala Arg Gln
             385              390              395

gca gcc aag aga gcc cgg gaa gtc acc cgg aag aaa tca ggc tta gaa       1248
Ala Ala Lys Arg Ala Arg Glu Val Thr Arg Lys Lys Ser Gly Leu Glu
             400              405              410

att agc aac cta cca ggt aaa tta gct gac tgt tct tcc aaa gat cct       1296
Ile Ser Asn Leu Pro Gly Lys Leu Ala Asp Cys Ser Ser Lys Asp Pro
415              420              425              430

gaa gaa tcc gaa ctc ttt att gta gaa ggg gat tca gct gga ggg tcg       1344
Glu Glu Ser Glu Leu Phe Ile Val Glu Gly Asp Ser Ala Gly Gly Ser
             435              440              445

gct aag caa ggt cgg tcc cgg gtt ttc cag gct att ttg ccg att cgt       1392
Ala Lys Gln Gly Arg Ser Arg Val Phe Gln Ala Ile Leu Pro Ile Arg
             450              455              460

ggt aag att ttg aat gtc gaa aaa gcc agc att gac cgt atc tta gcc       1440
Gly Lys Ile Leu Asn Val Glu Lys Ala Ser Ile Asp Arg Ile Leu Ala
             465              470              475

aat gaa gaa atc cgg tct ctc ttt aca gcc atg gga act ggc ttc ggg       1488
Asn Glu Glu Ile Arg Ser Leu Phe Thr Ala Met Gly Thr Gly Phe Gly
             480              485              490

gaa gaa ttt aat gtt gaa gaa gct cgc tac aat aag tta att atc atg       1536
Glu Glu Phe Asn Val Glu Glu Ala Arg Tyr Asn Lys Leu Ile Ile Met
495              500              505              510
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aca gat gct gat gtt gac gga gcc cac att cgg acc ttg ctc ttg acc      1584
Thr Asp Ala Asp Val Asp Gly Ala His Ile Arg Thr Leu Leu Leu Thr
            515             520                 525

ctt ctt tac cgg tat atg cgg ccc ttg att gaa gca ggt ttc gtc tac      1632
Leu Leu Tyr Arg Tyr Met Arg Pro Leu Ile Glu Ala Gly Phe Val Tyr
            530             535                 540

att gcc cag cca ccc ctc tac cag gtc aag caa ggc aag aag gtt aaa      1680
Ile Ala Gln Pro Pro Leu Tyr Gln Val Lys Gln Gly Lys Lys Val Lys
            545             550             555

tac ttt gat agt gac cgg gaa ctg gac tcc tac ttg aaa gaa att cct      1728
Tyr Phe Asp Ser Asp Arg Glu Leu Asp Ser Tyr Leu Lys Glu Ile Pro
        560             565             570

gac tca ccc aag cct tct gtc caa cgc tac aaa ggc tta gga gaa atg      1776
Asp Ser Pro Lys Pro Ser Val Gln Arg Tyr Lys Gly Leu Gly Glu Met
575             580             585                 590

gat gct gag cag ttg tgg gaa acc acc atg aac cca gaa cac cgc cgc      1824
Asp Ala Glu Gln Leu Trp Glu Thr Thr Met Asn Pro Glu His Arg Arg
            595             600                 605

tta ctt cgg gta gac gta gac gac gcc att gag gct gac act att ttt      1872
Leu Leu Arg Val Asp Val Asp Asp Ala Ile Glu Ala Asp Thr Ile Phe
            610             615                 620

gac atg ttg atg ggt gag gat gtc aaa ccc cgg cgc gac ttt atc aaa      1920
Asp Met Leu Met Gly Glu Asp Val Lys Pro Arg Arg Asp Phe Ile Lys
            625             630             635

gaa aat gcc cgt tac gtg gaa aat atc gat atc tag                      1956
Glu Asn Ala Arg Tyr Val Glu Asn Ile Asp Ile
        640             645
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<212> PRT
<213> Alloiococcus otitidis

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Lys Thr Tyr Asp Ala Ser Gln Ile Gln Val Leu Glu Gly Leu Glu Ala
            20              25                  30


Val Arg Val Arg Pro Gly Met Tyr Ile Gly Ser Thr Ser Lys Glu Gly
        35              40              45


Leu His His Leu Val Trp Glu Ile Val Asp Asn Ala Ile Asp Glu Ala
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<div style="text-align:center">50   55   60</div>

Met Ala Gly Tyr Ala Asp Lys Ile Ser Val Ser Ile Leu Glu Gly Asp
65   70   75   80

Val Ile Gln Val Ala Asp Asn Gly Arg Gly Ile Pro Val Asp Ile Gln
    85   90   95

Glu Lys Thr Gly Arg Pro Ala Val Glu Thr Val Phe Thr Val Leu His
    100   105   110

Ala Gly Gly Lys Phe Gly Gly Gly Gly Tyr Lys Val Ser Gly Gly Leu
    115   120   125

His Gly Val Gly Ser Ser Val Val Asn Ala Leu Ser Glu Tyr Leu Gln
    130   135   140

Val Gln Val His Arg Asp Gly Lys Ile Tyr Gln Gln Val Tyr Lys Arg
145   150   155   160

Gly Leu Val Asp Ser Asp Leu Glu Val Val Gly Glu Thr Asp His Thr
    165   170   175

Gly Thr Ile Val Thr Phe Lys Ala Asp Ser Leu Ile Phe Lys Asp Thr
    180   185   190

Thr Ser Tyr Asp Phe Asn Thr Leu Ala Thr Arg Ile Arg Glu Leu Ala
    195   200   205

Phe Leu Asn Arg Gly Leu Asn Ile Ser Ile Glu Asp Lys Arg Gln Ala
    210   215   220

Gly Gly Gln Ser Leu Asn Tyr His Tyr Glu Gly Gly Ile Ser Ser Tyr
225   230   235   240

Val Asp His Leu Asn Ser Ser Arg Glu Val Leu Tyr Glu Thr Pro Ile
    245   250   255

Phe Leu Glu Gly Glu Glu Glu Gly Ile Ser Val Glu Ile Ala Leu Gln
    260   265   270

His Thr Asp Ser Phe His Thr Asn Leu Met Ser Phe Ala Asn Asn Ile
    275   280   285

His Thr Tyr Glu Gly Gly Met His Ile Ser Gly Phe Lys Thr Ala Leu
    290   295   300

Thr Arg Ala Val Asn Asp Tyr Ala Arg Gln Asn Asn Leu Leu Arg Glu
305   310   315   320

Ser Glu Asp Asn Phe Thr Gly Asp Asp Val Arg Glu Gly Leu Thr Val
                325   330   335

Val Leu Ser Ile Lys His Pro Asp Pro Gln Phe Glu Gly Gln Thr Lys
                340   345   350

Thr Lys Leu Gly Asn Ser Glu Val Arg Gly Ile Ile Asp Arg Leu Phe
        355   360   365

Ser Gln His Phe Glu Arg Tyr Leu Met Glu Asn Pro Lys Val Gly Lys
    370   375   380

Arg Ile Val Asp Lys Ala Leu Leu Ala Ser Lys Ala Arg Gln Ala Ala
385   390   395   400

Lys Arg Ala Arg Glu Val Thr Arg Lys Lys Ser Gly Leu Glu Ile Ser
                405   410   415

Asn Leu Pro Gly Lys Leu Ala Asp Cys Ser Ser Lys Asp Pro Glu Glu
            420   425   430

Ser Glu Leu Phe Ile Val Glu Gly Asp Ser Ala Gly Gly Ser Ala Lys
        435   440   445

Gln Gly Arg Ser Arg Val Phe Gln Ala Ile Leu Pro Ile Arg Gly Lys
    450   455   460

Ile Leu Asn Val Glu Lys Ala Ser Ile Asp Arg Ile Leu Ala Asn Glu
465   470   475   480

Glu Ile Arg Ser Leu Phe Thr Ala Met Gly Thr Gly Phe Gly Glu Glu
                485   490   495

Phe Asn Val Glu Glu Ala Arg Tyr Asn Lys Leu Ile Ile Met Thr Asp
            500   505   510

Ala Asp Val Asp Gly Ala His Ile Arg Thr Leu Leu Leu Thr Leu Leu
        515   520   525

Tyr Arg Tyr Met Arg Pro Leu Ile Glu Ala Gly Phe Val Tyr Ile Ala
        530   535   540

Gln Pro Pro Leu Tyr Gln Val Lys Gln Gly Lys Lys Val Lys Tyr Phe
545   550   555   560

Asp Ser Asp Arg Glu Leu Asp Ser Tyr Leu Lys Glu Ile Pro Asp Ser
                565   570   575

Pro Lys Pro Ser Val Gln Arg Tyr Lys Gly Leu Gly Glu Met Asp Ala
            580   585   590

Glu Gln Leu Trp Glu Thr Thr Met Asn Pro Glu His Arg Arg Leu Leu
        595   600   605

Arg Val Asp Val Asp Asp Ala Ile Glu Ala Asp Thr Ile Phe Asp Met
    610   615   620

Leu Met Gly Glu Asp Val Lys Pro Arg Arg Asp Phe Ile Lys Glu Asn
625   630   635   640

Ala Arg Tyr Val Glu Asn Ile Asp Ile
            645

```
<210> 21
<211> 1218
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (16)..(1218)
<223>

<400> 21
agacctaatc atttt ttg aaa tgg aga aag aca aaa acc atc tat ggt ata          51
                Met Lys Trp Arg Lys Thr Lys Thr Ile Tyr Gly Ile
                 1               5                   10

ctt aag aac aaa agg aag ttt gga ggg att ttt ttg aaa ttt tca gta          99
Leu Lys Asn Lys Arg Lys Phe Gly Gly Ile Phe Leu Lys Phe Ser Val
        15                  20                  25

aaa cgg acg gaa ttt cta aaa gta tta aaa aaa gta cag att gca gtg         147
```

```
Lys Arg Thr Glu Phe Leu Lys Val Leu Lys Lys Val Gln Ile Ala Val
    30                  35              40
```

```
tct tct aaa agt acc atc gct atc ttg acc ggg att aaa tta gaa gcg          195
Ser Ser Lys Ser Thr Ile Ala Ile Leu Thr Gly Ile Lys Leu Glu Ala
45                  50                  55                  60
```

```
gat aac cag ggt tta acc tta acc gga tct aac tcg gat atc tca gtt          243
Asp Asn Gln Gly Leu Thr Leu Thr Gly Ser Asn Ser Asp Ile Ser Val
                    65                  70                  75
```

```
gaa agt tac tta tct gtg acc gat gaa ggg gcg gat ttg gtt att gat          291
Glu Ser Tyr Leu Ser Val Thr Asp Glu Gly Ala Asp Leu Val Ile Asp
                80                  85                  90
```

```
gag ccg ggg cag att gtc ttg caa cca gcc cgg tta ttt gcc aat atc          339
Glu Pro Gly Gln Ile Val Leu Gln Pro Ala Arg Leu Phe Ala Asn Ile
            95                  100                 105
```

```
gtc caa aaa tta ccg gac acc cac ttt aag gta aac gtt agc caa ggc          387
Val Gln Lys Leu Pro Asp Thr His Phe Lys Val Asn Val Ser Gln Gly
        110                 115                 120
```

```
cag caa acc caa atc acc tca gct tca gcc tcc ttt act atc aac ggc          435
Gln Gln Thr Gln Ile Thr Ser Ala Ser Ala Ser Phe Thr Ile Asn Gly
125                 130                 135                 140
```

```
att gac gcc atg tcc tac ccc cac ttg cca gat atc gac ctg gag gaa          483
Ile Asp Ala Met Ser Tyr Pro His Leu Pro Asp Ile Asp Leu Glu Glu
                    145                 150                 155
```

```
tcc ttt acc ctg ccg gtt gac ctc ttt aaa aac atg atc aac cag act          531
Ser Phe Thr Leu Pro Val Asp Leu Phe Lys Asn Met Ile Asn Gln Thr
                160                 165                 170
```

```
gtc atc gca gtc tcc aac cat gaa agt cgg ccc atc cta act ggg gtt          579
Val Ile Ala Val Ser Asn His Glu Ser Arg Pro Ile Leu Thr Gly Val
            175                 180                 185
```

```
aac cta tct ctc aaa gag ggc cga ctc aag gca gtg gca acc gac agc          627
Asn Leu Ser Leu Lys Glu Gly Arg Leu Lys Ala Val Ala Thr Asp Ser
        190                 195                 200
```

```
cac cgt ttg tcg caa cgg tcc atc caa tta gag tca gcg cct gat att          675
His Arg Leu Ser Gln Arg Ser Ile Gln Leu Glu Ser Ala Pro Asp Ile
205                 210                 215                 220
```

```
tcc ttt gac att gtg ata cca ggt aag tct ttg act gaa ctg act aag          723
Ser Phe Asp Ile Val Ile Pro Gly Lys Ser Leu Thr Glu Leu Thr Lys
                    225                 230                 235
```

```
ttg atg gat gca gat gaa gaa gtc cgg gta gcc atc agc gac aac caa          771
Leu Met Asp Ala Asp Glu Glu Val Arg Val Ala Ile Ser Asp Asn Gln
                    240                 245                 250
```

```
atc cta ttt gcc ctc tcc agc agc cag ttt tac tct cgg ctc cta gaa          819
Ile Leu Phe Ala Leu Ser Ser Ser Gln Phe Tyr Ser Arg Leu Leu Glu
```

	255					260					265					

```
            255                 260                 265
ggt aag tat cct gat acc gac cgc ttg atc cca ggc gac acc cca acg        867
Gly Lys Tyr Pro Asp Thr Asp Arg Leu Ile Pro Gly Asp Thr Pro Thr
        270                 275                 280

gaa atc acc ttg gac acc aag gaa tta cag ggg gct gtt gac cgg gct        915
Glu Ile Thr Leu Asp Thr Lys Glu Leu Gln Gly Ala Val Asp Arg Ala
285                 290                 295                 300

tcc ctc ctc tcc cat gaa ggg aaa aac aat gtg gtc caa ctc aca gtg        963
Ser Leu Leu Ser His Glu Gly Lys Asn Asn Val Val Gln Leu Thr Val
                305                 310                 315

act gct gaa aag ttg gaa atc gaa ggc cag tca gct gaa gtg ggc cat       1011
Thr Ala Glu Lys Leu Glu Ile Glu Gly Gln Ser Ala Glu Val Gly His
                320                 325                 330

gtc caa gaa gaa att gac ttt ggc cac ttc caa ggc caa gac tta acc       1059
Val Gln Glu Glu Ile Asp Phe Gly His Phe Gln Gly Gln Asp Leu Thr
                335                 340                 345

att tct ttc aac ccc gac tac tta aaa gag gcc ttg gct acc ttt ggt       1107
Ile Ser Phe Asn Pro Asp Tyr Leu Lys Glu Ala Leu Ala Thr Phe Gly
        350                 355                 360

caa gga gaa att aag ttg aaa tta gtt tcg acc ttg cga ccc ttt gtc       1155
Gln Gly Glu Ile Lys Leu Lys Leu Val Ser Thr Leu Arg Pro Phe Val
365                 370                 375                 380

atc gtc cca agt gag gac caa gga gac ttt atc caa ctt att act cca       1203
Ile Val Pro Ser Glu Asp Gln Gly Asp Phe Ile Gln Leu Ile Thr Pro
                385                 390                 395

atc cga aca gcc taa                                                    1218
Ile Arg Thr Ala
                400


<210> 22
<211> 400
<212> PRT
<213> Alloiococcus otitidis

<400> 22
Met Lys Trp Arg Lys Thr Lys Thr Ile Tyr Gly Ile Leu Lys Asn Lys
1               5                   10                  15


Arg Lys Phe Gly Gly Ile Phe Leu Lys Phe Ser Val Lys Arg Thr Glu
            20                  25                  30


Phe Leu Lys Val Leu Lys Lys Val Gln Ile Ala Val Ser Ser Lys Ser
        35                  40                  45
```

Thr Ile Ala Ile Leu Thr Gly Ile Lys Leu Glu Ala Asp Asn Gln Gly
    50   55   60

Leu Thr Leu Thr Gly Ser Asn Ser Asp Ile Ser Val Glu Ser Tyr Leu
65   70   75   80

Ser Val Thr Asp Glu Gly Ala Asp Leu Val Ile Asp Glu Pro Gly Gln
            85   90   95

Ile Val Leu Gln Pro Ala Arg Leu Phe Ala Asn Ile Val Gln Lys Leu
            100   105   110

Pro Asp Thr His Phe Lys Val Asn Val Ser Gln Gly Gln Gln Thr Gln
        115   120   125

Ile Thr Ser Ala Ser Ala Ser Phe Thr Ile Asn Gly Ile Asp Ala Met
    130   135   140

Ser Tyr Pro His Leu Pro Asp Ile Asp Leu Glu Glu Ser Phe Thr Leu
145   150   155   160

Pro Val Asp Leu Phe Lys Asn Met Ile Asn Gln Thr Val Ile Ala Val
            165   170   175

Ser Asn His Glu Ser Arg Pro Ile Leu Thr Gly Val Asn Leu Ser Leu
        180   185   190

Lys Glu Gly Arg Leu Lys Ala Val Ala Thr Asp Ser His Arg Leu Ser
        195   200   205

Gln Arg Ser Ile Gln Leu Glu Ser Ala Pro Asp Ile Ser Phe Asp Ile
    210   215   220

Val Ile Pro Gly Lys Ser Leu Thr Glu Leu Thr Lys Leu Met Asp Ala
225   230   235   240

Asp Glu Glu Val Arg Val Ala Ile Ser Asp Asn Gln Ile Leu Phe Ala
            245   250   255

Leu Ser Ser Ser Gln Phe Tyr Ser Arg Leu Leu Glu Gly Lys Tyr Pro
        260   265   270

Asp Thr Asp Arg Leu Ile Pro Gly Asp Thr Pro Thr Glu Ile Thr Leu

```
                275                    280                      285

        Asp Thr Lys Glu Leu Gln Gly Ala Val Asp Arg Ala Ser Leu Leu Ser
            290                    295                  300

        His Glu Gly Lys Asn Asn Val Val Gln Leu Thr Val Thr Ala Glu Lys
        305                    310                  315                320

        Leu Glu Ile Glu Gly Gln Ser Ala Glu Val Gly His Val Gln Glu Glu
                        325                  330                  335

        Ile Asp Phe Gly His Phe Gln Gly Gln Asp Leu Thr Ile Ser Phe Asn
                    340                    345                  350

        Pro Asp Tyr Leu Lys Glu Ala Leu Ala Thr Phe Gly Gln Gly Glu Ile
                    355                    360                  365

        Lys Leu Lys Leu Val Ser Thr Leu Arg Pro Phe Val Ile Val Pro Ser
            370                    375                  380

        Glu Asp Gln Gly Asp Phe Ile Gln Leu Ile Thr Pro Ile Arg Thr Ala
        385                    390                  395                400
```

<210> 23
<211> 1317
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (25)..(1317)
<223>

<400> 23

```
tcaataactg cttttttagg agct ttg cag atg aat tgg aaa gaa acc atc          51
                          Met Gln Met Asn Trp Lys Glu Thr Ile
                          1                   5

agt ctc atc aac acc acc cgg ggg acc gga gac aag aaa aat ttg aac         99
Ser Leu Ile Asn Thr Thr Arg Gly Thr Gly Asp Lys Lys Asn Leu Asn
10                   15                  20                  25

cgg atg cga ctt tta ctc aaa gag cta ggt aat cct gaa aca gac ttg        147
Arg Met Arg Leu Leu Leu Lys Glu Leu Gly Asn Pro Glu Thr Asp Leu
                30                    35                  40
```

```
ccg gtc atc cac gtt gct ggc acc aat ggc aaa ggg acg acc tgt gct      195
Pro Val Ile His Val Ala Gly Thr Asn Gly Lys Gly Thr Thr Cys Ala
            45                    50                    55

tat att gcc cac agc ttg gcc cgt gct ggt tat aaa aca gga ctt tac      243
Tyr Ile Ala His Ser Leu Ala Arg Ala Gly Tyr Lys Thr Gly Leu Tyr
            60                    65                    70

acc agc ccc cac ctg gag cgg gtc aat gaa cgg atc cgg att aat gac      291
Thr Ser Pro His Leu Glu Arg Val Asn Glu Arg Ile Arg Ile Asn Asp
            75                    80                    85

cgc tac ata tcc gac caa gac tta atg gct ttg acc ggt caa att gcc      339
Arg Tyr Ile Ser Asp Gln Asp Leu Met Ala Leu Thr Gly Gln Ile Ala
90                    95                    100                   105

ccc atc att gac cat cta gaa gac tgc ttg ggt gag aaa tac tat tct      387
Pro Ile Ile Asp His Leu Glu Asp Cys Leu Gly Glu Lys Tyr Tyr Ser
                      110                   115                   120

ttt gaa att tta act gcc ctt gcc ttc ttg tac ttc cag caa gca ggg      435
Phe Glu Ile Leu Thr Ala Leu Ala Phe Leu Tyr Phe Gln Gln Ala Gly
                      125                   130                   135

gtg gac ttt tta gtt tta gaa act ggg gta ggg gga aaa att gat gcg      483
Val Asp Phe Leu Val Leu Glu Thr Gly Val Gly Gly Lys Ile Asp Ala
            140                   145                   150

acc aat gtg gtg ccc gct cca ctg gtc tca gtc att atc tct att ggc      531
Thr Asn Val Val Pro Ala Pro Leu Val Ser Val Ile Ile Ser Ile Gly
            155                   160                   165

tat gac cac acc cat gtc ttg ggt aat acc ctg gaa gac att acc cgg      579
Tyr Asp His Thr His Val Leu Gly Asn Thr Leu Glu Asp Ile Thr Arg
170                   175                   180                   185

cac aag gca ggg att att aag aaa ggc tgt ccg gtg gtg gtg ggc cct      627
His Lys Ala Gly Ile Ile Lys Lys Gly Cys Pro Val Val Val Gly Pro
                      190                   195                   200

ctt gcc gac cat tta ttg gct att gtt aaa gag gtg tcc aaa gaa atg      675
Leu Ala Asp His Leu Leu Ala Ile Val Lys Glu Val Ser Lys Glu Met
                      205                   210                   215

gac agt aat tta acc att gtc cat ccc gac aag ttt gac att gtt cat      723
Asp Ser Asn Leu Thr Ile Val His Pro Asp Lys Phe Asp Ile Val His
            220                   225                   230

caa acc ctt gac tac cag tcc ttt aaa tac ggt ggg gac ttg gtt tta      771
Gln Thr Leu Asp Tyr Gln Ser Phe Lys Tyr Gly Gly Asp Leu Val Leu
            235                   240                   245

gag act caa atg att ggt aac cac cag ctg gta aac act gcc cta gct      819
Glu Thr Gln Met Ile Gly Asn His Gln Leu Val Asn Thr Ala Leu Ala
250                   255                   260                   265

tat gaa gcc ttg aag att gtc caa caa tct tac ccc gat ttg aca gat      867
```

```
Tyr Glu Ala Leu Lys Ile Val Gln Gln Ser Tyr Pro Asp Leu Thr Asp
        270             275             280

tta gat ata tta gaa ggc ttg aag acg acc cac tgg cca ggc cgg atg    915
Leu Asp Ile Leu Glu Gly Leu Lys Thr Thr His Trp Pro Gly Arg Met
        285             290             295

caa aag cta tct gac cag cca gtg gtt gtt ctt gat ggg gcc cac aac    963
Gln Lys Leu Ser Asp Gln Pro Val Val Val Leu Asp Gly Ala His Asn
        300             305             310

gaa atc ggg gtc aag gct ctt aga cag tca att gac cac ttt ttc ccc   1011
Glu Ile Gly Val Lys Ala Leu Arg Gln Ser Ile Asp His Phe Phe Pro
        315             320             325

ggc aaa aaa atc acc tat ttt gcc gga atg atg gtc gaa aaa gac ttc   1059
Gly Lys Lys Ile Thr Tyr Phe Ala Gly Met Met Val Glu Lys Asp Phe
330             335             340             345

gcc aaa atg ttt gac ctc ctg ggg gaa aca gct gat aaa ttt tac ttg   1107
Ala Lys Met Phe Asp Leu Leu Gly Glu Thr Ala Asp Lys Phe Tyr Leu
            350             355             360

att tca ccc gat ttg act cgc ggt ttt gat gtc gac caa gcc gtt caa   1155
Ile Ser Pro Asp Leu Thr Arg Gly Phe Asp Val Asp Gln Ala Val Gln
            365             370             375

tct ttg act gac aag ggc tac cag gct tcc agt gtg gct agc ctc caa   1203
Ser Leu Thr Asp Lys Gly Tyr Gln Ala Ser Ser Val Ala Ser Leu Gln
            380             385             390

gcc atc tta gac tac ata aac cag caa gca aaa gca gat gaa att atc   1251
Ala Ile Leu Asp Tyr Ile Asn Gln Gln Ala Lys Ala Asp Glu Ile Ile
            395             400             405

att atc ttt ggc tcc ctc tac ttg gtt ggc gac ttc cta aaa ctt tac   1299
Ile Ile Phe Gly Ser Leu Tyr Leu Val Gly Asp Phe Leu Lys Leu Tyr
410             415             420             425

cat gaa gca tcc ggt taa                                           1317
His Glu Ala Ser Gly
            430
```

```
<210> 24
<211> 430
<212> PRT
<213> Alloiococcus otitidis

<400> 24
Met Gln Met Asn Trp Lys Glu Thr Ile Ser Leu Ile Asn Thr Thr Arg
1               5               10              15


Gly Thr Gly Asp Lys Lys Asn Leu Asn Arg Met Arg Leu Leu Leu Lys
            20              25              30
```

Glu Leu Gly Asn Pro Glu Thr Asp Leu Pro Val Ile His Val Ala Gly
          35   40   45

Thr Asn Gly Lys Gly Thr Thr Cys Ala Tyr Ile Ala His Ser Leu Ala
          50   55   60

Arg Ala Gly Tyr Lys Thr Gly Leu Tyr Thr Ser Pro His Leu Glu Arg
65   70   75   80

Val Asn Glu Arg Ile Arg Ile Asn Asp Arg Tyr Ile Ser Asp Gln Asp
                    85   90   95

Leu Met Ala Leu Thr Gly Gln Ile Ala Pro Ile Ile Asp His Leu Glu
              100   105   110

Asp Cys Leu Gly Glu Lys Tyr Tyr Ser Phe Glu Ile Leu Thr Ala Leu
          115   120   125

Ala Phe Leu Tyr Phe Gln Gln Ala Gly Val Asp Phe Leu Val Leu Glu
          130   135   140

Thr Gly Val Gly Gly Lys Ile Asp Ala Thr Asn Val Val Pro Ala Pro
145   150   155   160

Leu Val Ser Val Ile Ile Ser Ile Gly Tyr Asp His Thr His Val Leu
                    165   170   175

Gly Asn Thr Leu Glu Asp Ile Thr Arg His Lys Ala Gly Ile Ile Lys
              180   185   190

Lys Gly Cys Pro Val Val Val Gly Pro Leu Ala Asp His Leu Leu Ala
          195   200   205

Ile Val Lys Glu Val Ser Lys Glu Met Asp Ser Asn Leu Thr Ile Val
          210   215   220

His Pro Asp Lys Phe Asp Ile Val His Gln Thr Leu Asp Tyr Gln Ser
225   230   235   240

Phe Lys Tyr Gly Gly Asp Leu Val Leu Glu Thr Gln Met Ile Gly Asn
              245   250   255

His Gln Leu Val Asn Thr Ala Leu Ala Tyr Glu Ala Leu Lys Ile Val
        260   265   270

Gln Gln Ser Tyr Pro Asp Leu Thr Asp Leu Asp Ile Leu Glu Gly Leu
        275   280   285

Lys Thr Thr His Trp Pro Gly Arg Met Gln Lys Leu Ser Asp Gln Pro
        290   295   300

Val Val Val Leu Asp Gly Ala His Asn Glu Ile Gly Val Lys Ala Leu
305   310   315   320

Arg Gln Ser Ile Asp His Phe Phe Pro Gly Lys Lys Ile Thr Tyr Phe
        325   330   335

Ala Gly Met Met Val Glu Lys Asp Phe Ala Lys Met Phe Asp Leu Leu
        340   345   350

Gly Glu Thr Ala Asp Lys Phe Tyr Leu Ile Ser Pro Asp Leu Thr Arg
        355   360   365

Gly Phe Asp Val Asp Gln Ala Val Gln Ser Leu Thr Asp Lys Gly Tyr
        370   375   380

Gln Ala Ser Ser Val Ala Ser Leu Gln Ala Ile Leu Asp Tyr Ile Asn
385   390   395   400

Gln Gln Ala Lys Ala Asp Glu Ile Ile Ile Ile Phe Gly Ser Leu Tyr
        405   410   415

Leu Val Gly Asp Phe Leu Lys Leu Tyr His Glu Ala Ser Gly
        420   425   430

```
<210> 25
<211> 1653
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (91)..(1653)
<223>

<400> 25
cttcttgttt cattttttaat cttatctgaa acaaatgatt tttcaactct tttttatctt        60
```

```
actttaaaag ttttagttag gagccttagc ttg tac cgt atc tct atg aaa gac      114
                                      Met Tyr Arg Ile Ser Met Lys Asp.
                                      1               5

ttg cat gcc cta tta gct agc aag cag cag ttg aaa gaa gtg gtc ggt        162
Leu His Ala Leu Leu Ala Ser Lys Gln Gln Leu Lys Glu Val Val Gly
    10              15                  20

ccc gac caa gtt tgg cat tac aat ttg cct caa ggg gaa ttg gcc gac        210
Pro Asp Gln Val Trp His Tyr Asn Leu Pro Gln Gly Glu Leu Ala Asp
25              30                  35                  40

caa gtt ttt gac aaa ctt tcc tac aat tcc caa act gcc tcc tca gac        258
Gln Val Phe Asp Lys Leu Ser Tyr Asn Ser Gln Thr Ala Ser Ser Asp
                45                  50                  55

acc ctt ttc ttt tgc aag ggt gct tcc ttt aaa aga gac tac cta gcc       306
Thr Leu Phe Phe Cys Lys Gly Ala Ser Phe Lys Arg Asp Tyr Leu Ala
                60                  65                  70

cag gcg gtt gac cag ggt gtc caa gtc tat att tcc gaa aaa ttg tat        354
Gln Ala Val Asp Gln Gly Val Gln Val Tyr Ile Ser Glu Lys Leu Tyr
            75                  80                  85

caa ggc ctg gat gct tat gcc atc att gtc cgt gac atc cgc cag acc        402
Gln Gly Leu Asp Ala Tyr Ala Ile Ile Val Arg Asp Ile Arg Gln Thr
        90                  95                  100

atg gcc cta gtc gct aag gct ttt tac cag gct cca gat gaa aaa ttg        450
Met Ala Leu Val Ala Lys Ala Phe Tyr Gln Ala Pro Asp Glu Lys Leu
105                 110                 115                 120

acc ctg att ggc att acc ggg acc aag ggc aag aca acc aca agt tac        498
Thr Leu Ile Gly Ile Thr Gly Thr Lys Gly Lys Thr Thr Thr Ser Tyr
                125                 130                 135

ctc ctc aaa tcc atc ctg gac cag gac caa gcc ggt aag aca gct att       546
Leu Leu Lys Ser Ile Leu Asp Gln Asp Gln Ala Gly Lys Thr Ala Ile
                140                 145                 150

att tca acc ttg ggg att tcc tta gac ggc cag acc caa gaa gaa gcc       594
Ile Ser Thr Leu Gly Ile Ser Leu Asp Gly Gln Thr Gln Glu Glu Ala
                155                 160                 165

tcc ctg acc act cct gaa gcc ttg gac ctc tac cag atg att gcc cgg       642
Ser Leu Thr Thr Pro Glu Ala Leu Asp Leu Tyr Gln Met Ile Ala Arg
170                 175                 180

gcc caa gac cag ggg atg gac caa ttg att atg gaa gta tct agc caa       690
Ala Gln Asp Gln Gly Met Asp Gln Leu Ile Met Glu Val Ser Ser Gln
185                 190                 195                 200

gcc tac aag atg gac cgg gtc tat gga ctg act ttc gac ttt gga gcc       738
Ala Tyr Lys Met Asp Arg Val Tyr Gly Leu Thr Phe Asp Phe Gly Ala
                205                 210                 215
```

```
ttc tta aat att tcg cct gac cat atc ggc cct aat gag cac cca gat        786
Phe Leu Asn Ile Ser Pro Asp His Ile Gly Pro Asn Glu His Pro Asp
            220                 225                 230

atg gaa gat tac ttc tat tgt aaa agt cgt ttg gtt aaa cat tcc aag        834
Met Glu Asp Tyr Phe Tyr Cys Lys Ser Arg Leu Val Lys His Ser Lys
            235                 240                 245

ttg gcc ttg ctc aac gct gga ctt gac cag cta gac tac tta aaa gac        882
Leu Ala Leu Leu Asn Ala Gly Leu Asp Gln Leu Asp Tyr Leu Lys Asp
    250                 255                 260

ctt agc caa aaa aat ggc ggt cag gtc caa gtt tac ggc caa gat ccc        930
Leu Ser Gln Lys Asn Gly Gly Gln Val Gln Val Tyr Gly Gln Asp Pro
265                 270                 275                 280

aag act tgt gac tac tat ttt gag gtt aac aac cag gac agc cgc cgc        978
Lys Thr Cys Asp Tyr Tyr Phe Glu Val Asn Asn Gln Asp Ser Arg Arg
            285                 290                 295

ttt gcc att aaa agc caa agc cct gat gac ttg gcc att gat ggg gat       1026
Phe Ala Ile Lys Ser Gln Ser Pro Asp Asp Leu Ala Ile Asp Gly Asp
            300                 305                 310

tac caa ttt gaa atg ttg ggt gat ttt aac aag gag aat gcc ctt tgt       1074
Tyr Gln Phe Glu Met Leu Gly Asp Phe Asn Lys Glu Asn Ala Leu Cys
            315                 320                 325

gcc gct ctt ata gcg ggg cat tta gaa gtt ggg caa gag gcc att tac       1122
Ala Ala Leu Ile Ala Gly His Leu Glu Val Gly Gln Glu Ala Ile Tyr
    330                 335                 340

caa gga ata gcc cag gcc caa gtg cca gga cgg atg cag cat tat act       1170
Gln Gly Ile Ala Gln Ala Gln Val Pro Gly Arg Met Gln His Tyr Thr
345                 350                 355                 360

tat ggc aac aat cac atc tat gta gac ttt gcc cac aat tac atc agc       1218
Tyr Gly Asn Asn His Ile Tyr Val Asp Phe Ala His Asn Tyr Ile Ser
            365                 370                 375

ttg aaa aat ctt ttt gat ttt gcc caa gac caa cac ccg gac cac acc       1266
Leu Lys Asn Leu Phe Asp Phe Ala Gln Asp Gln His Pro Asp His Thr
            380                 385                 390

atg gtg gtt gtc ttg ggg gcc cct ggc aac aag ggg gtg tct cgc cgc       1314
Met Val Val Val Leu Gly Ala Pro Gly Asn Lys Gly Val Ser Arg Arg
            395                 400                 405

aag gat atg gga tac ttg ctg tcc caa tac caa ggg gaa gtt atc ttg       1362
Lys Asp Met Gly Tyr Leu Leu Ser Gln Tyr Gln Gly Glu Val Ile Leu
    410                 415                 420

acc gaa gat gac ccc aat ttt gaa gac gtt caa gct atc tgc caa gaa       1410
Thr Glu Asp Asp Pro Asn Phe Glu Asp Val Gln Ala Ile Cys Gln Glu
425                 430                 435                 440
```

```
att gcc caa tac att gat ggc ccc atc cag gtg acc ttt aat gat aac      1458
Ile Ala Gln Tyr Ile Asp Gly Pro Ile Gln Val Thr Phe Asn Asp Asn
                445             450             455

cgg ata aat gcc atc caa gac ctc cta gag tcc tta acc cca gaa agt      1506
Arg Ile Asn Ala Ile Gln Asp Leu Leu Glu Ser Leu Thr Pro Glu Ser
                460             465             470

caa aaa gtc atc ctg ctt gca ggc aag ggg tcc gac cag tac atg ctg      1554
Gln Lys Val Ile Leu Leu Ala Gly Lys Gly Ser Asp Gln Tyr Met Leu
                475             480             485

cgg cgg ggt gtg aag gaa gat tat gcg gga gac cac aaa ttg gtt gaa      1602
Arg Arg Gly Val Lys Glu Asp Tyr Ala Gly Asp His Lys Leu Val Glu
    490             495             500

gca ttt tta aac cag caa aag act tct tct cat gag aag ctt gag ggt      1650
Ala Phe Leu Asn Gln Gln Lys Thr Ser Ser His Glu Lys Leu Glu Gly
505             510             515             520

tag                                                                  1653
```

```
<210> 26
<211> 520
<212> PRT
<213> Alloiococcus otitidis

<400> 26
Met Tyr Arg Ile Ser Met Lys Asp Leu His Ala Leu Leu Ala Ser Lys
1               5               10              15


Gln Gln Leu Lys Glu Val Val Gly Pro Asp Gln Val Trp His Tyr Asn
                20              25              30


Leu Pro Gln Gly Glu Leu Ala Asp Gln Val Phe Asp Lys Leu Ser Tyr
        35              40              45


Asn Ser Gln Thr Ala Ser Ser Asp Thr Leu Phe Phe Cys Lys Gly Ala
        50              55              60


Ser Phe Lys Arg Asp Tyr Leu Ala Gln Ala Val Asp Gln Gly Val Gln
65              70              75              80


Val Tyr Ile Ser Glu Lys Leu Tyr Gln Gly Leu Asp Ala Tyr Ala Ile
                85              90              95


Ile Val Arg Asp Ile Arg Gln Thr Met Ala Leu Val Ala Lys Ala Phe
                100             105             110
```

```
Tyr Gln Ala Pro Asp Glu Lys Leu Thr Leu Ile Gly Ile Thr Gly Thr
        115             120             125

Lys Gly Lys Thr Thr Thr Ser Tyr Leu Leu Lys Ser Ile Leu Asp Gln
        130             135             140

Asp Gln Ala Gly Lys Thr Ala Ile Ile Ser Thr Leu Gly Ile Ser Leu
145             150             155             160

Asp Gly Gln Thr Gln Glu Glu Ala Ser Leu Thr Thr Pro Glu Ala Leu
                165             170             175

Asp Leu Tyr Gln Met Ile Ala Arg Ala Gln Asp Gln Gly Met Asp Gln
            180             185             190

Leu Ile Met Glu Val Ser Ser Gln Ala Tyr Lys Met Asp Arg Val Tyr
            195             200             205

Gly Leu Thr Phe Asp Phe Gly Ala Phe Leu Asn Ile Ser Pro Asp His
    210             215             220

Ile Gly Pro Asn Glu His Pro Asp Met Glu Asp Tyr Phe Tyr Cys Lys
225             230             235             240

Ser Arg Leu Val Lys His Ser Lys Leu Ala Leu Leu Asn Ala Gly Leu
            245             250             255

Asp Gln Leu Asp Tyr Leu Lys Asp Leu Ser Gln Lys Asn Gly Gly Gln
            260             265             270

Val Gln Val Tyr Gly Gln Asp Pro Lys Thr Cys Asp Tyr Tyr Phe Glu
        275             280             285

Val Asn Asn Gln Asp Ser Arg Arg Phe Ala Ile Lys Ser Gln Ser Pro
    290             295             300

Asp Asp Leu Ala Ile Asp Gly Asp Tyr Gln Phe Glu Met Leu Gly Asp
305             310             315             320

Phe Asn Lys Glu Asn Ala Leu Cys Ala Ala Leu Ile Ala Gly His Leu
            325             330             335

Glu Val Gly Gln Glu Ala Ile Tyr Gln Gly Ile Ala Gln Ala Gln Val
```

```
                      340                    345                    350


        Pro Gly Arg Met Gln His Tyr Thr Tyr Gly Asn Asn His Ile Tyr Val
              355                    360                    365

        Asp Phe Ala His Asn Tyr Ile Ser Leu Lys Asn Leu Phe Asp Phe Ala
              370                    375                    380

        Gln Asp Gln His Pro Asp His Thr Met Val Val Val Leu Gly Ala Pro
        385                    390                    395                    400

        Gly Asn Lys Gly Val Ser Arg Arg Lys Asp Met Gly Tyr Leu Leu Ser
                            405                    410                    415

        Gln Tyr Gln Gly Glu Val Ile Leu Thr Glu Asp Asp Pro Asn Phe Glu
                      420                    425                    430

        Asp Val Gln Ala Ile Cys Gln Glu Ile Ala Gln Tyr Ile Asp Gly Pro
              435                    440                    445

        Ile Gln Val Thr Phe Asn Asp Asn Arg Ile Asn Ala Ile Gln Asp Leu
              450                    455                    460

        Leu Glu Ser Leu Thr Pro Glu Ser Gln Lys Val Ile Leu Leu Ala Gly
        465                    470                    475                    480

        Lys Gly Ser Asp Gln Tyr Met Leu Arg Arg Gly Val Lys Glu Asp Tyr
                            485                    490                    495

        Ala Gly Asp His Lys Leu Val Glu Ala Phe Leu Asn Gln Gln Lys Thr
                      500                    505                    510

        Ser Ser His Glu Lys Leu Glu Gly
              515                    520
```

<210> 27
<211> 636
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (25)..(636)
<223>

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<400> 27
aggactgaaa ggaaggttgg agtc atg aag tgg ttg agt cgg atc ttg att          51
                           Met Lys Trp Leu Ser Arg Ile Leu Ile
                           1               5

gtt gtt ggg ata ggc ttt ctg att gcc ttt ggc tac acg att tat gac       99
Val Val Gly Ile Gly Phe Leu Ile Ala Phe Gly Tyr Thr Ile Tyr Asp
10                   15                  20                  25

cat gct aac tcg aca tcg gtt acc cta gaa gaa gcc cag gtg gcc ctg       147
His Ala Asn Ser Thr Ser Val Thr Leu Glu Glu Ala Gln Val Ala Leu
                 30                  35                  40

gaa gaa agc cgg gcc cag gct gct gaa gct ggg gac ggg gac cag gat       195
Glu Glu Ser Arg Ala Gln Ala Ala Glu Ala Gly Asp Gly Asp Gln Asp
             45                  50                  55

ggc caa gat ggg gcg agt gac atc gat atc caa aac tac cag cct gaa       243
Gly Gln Asp Gly Ala Ser Asp Ile Asp Ile Gln Asn Tyr Gln Pro Glu
                 60                  65                  70

gct ggg gag gct ttt ggg gtc tta gat att ccc aaa ctc gac cgg agc       291
Ala Gly Glu Ala Phe Gly Val Leu Asp Ile Pro Lys Leu Asp Arg Ser
         75                  80                  85

att ggc att gta gcc gga acg gat gca gac tct ctt aag aag ggg gta       339
Ile Gly Ile Val Ala Gly Thr Asp Ala Asp Ser Leu Lys Lys Gly Val
90                  95                  100                 105

ggt cac gtt gag aat aca gtc ttc cct ggc caa ggc gaa caa att gtc       387
Gly His Val Glu Asn Thr Val Phe Pro Gly Gln Gly Glu Gln Ile Val
                 110                 115                 120

ctc tct ggc cac cgg gat acc gtc ttc cgg gac ttt ggc gaa tta gaa       435
Leu Ser Gly His Arg Asp Thr Val Phe Arg Asp Phe Gly Glu Leu Glu
             125                 130                 135

att ggc gac aat ttt atc gtt caa atg cct tac ggg gac tat gaa tat       483
Ile Gly Asp Asn Phe Ile Val Gln Met Pro Tyr Gly Asp Tyr Glu Tyr
         140                 145                 150

gag att cag gac tat gaa att gtc gac cgg gat gat acc tcc gtc atc       531
Glu Ile Gln Asp Tyr Glu Ile Val Asp Arg Asp Asp Thr Ser Val Ile
         155                 160                 165

cgg cct atg ggg gaa gaa gtc tta gtg gtt tca acc tgc tac ccc ttt       579
Arg Pro Met Gly Glu Glu Val Leu Val Val Ser Thr Cys Tyr Pro Phe
170                 175                 180                 185

gaa ttt tac ggt ttt gcc cct gac cgc ttt gtt ttc tat tgt tac ccc       627
Glu Phe Tyr Gly Phe Ala Pro Asp Arg Phe Val Phe Tyr Cys Tyr Pro
                 190                 195                 200

gtt gaa taa                                                            636
Val Glu
```

```
<210> 28
<211> 203
<212> PRT
<213> Alloiococcus otitidis

<400> 28
Met Lys Trp Leu Ser Arg Ile Leu Ile Val Val Gly Ile Gly Phe Leu
1               5                   10                  15


Ile Ala Phe Gly Tyr Thr Ile Tyr Asp His Ala Asn Ser Thr Ser Val
                20                  25                  30


Thr Leu Glu Glu Ala Gln Val Ala Leu Glu Glu Ser Arg Ala Gln Ala
        35                  40                  45


Ala Glu Ala Gly Asp Gly Asp Gln Asp Gly Gln Asp Gly Ala Ser Asp
        50                  55                  60


Ile Asp Ile Gln Asn Tyr Gln Pro Glu Ala Gly Glu Ala Phe Gly Val
65                  70                  75                  80


Leu Asp Ile Pro Lys Leu Asp Arg Ser Ile Gly Ile Val Ala Gly Thr
                85                  90                  95


Asp Ala Asp Ser Leu Lys Lys Gly Val Gly His Val Glu Asn Thr Val
                100                 105                 110


Phe Pro Gly Gln Gly Glu Gln Ile Val Leu Ser Gly His Arg Asp Thr
            115                 120                 125


Val Phe Arg Asp Phe Gly Glu Leu Glu Ile Gly Asp Asn Phe Ile Val
        130                 135                 140


Gln Met Pro Tyr Gly Asp Tyr Glu Tyr Glu Ile Gln Asp Tyr Glu Ile
145                 150                 155                 160


Val Asp Arg Asp Asp Thr Ser Val Ile Arg Pro Met Gly Glu Glu Val
                165                 170                 175


Leu Val Val Ser Thr Cys Tyr Pro Phe Glu Phe Tyr Gly Phe Ala Pro
                180                 185                 190


Asp Arg Phe Val Phe Tyr Cys Tyr Pro Val Glu
            195                 200
```

<210> 29
<211> 1290
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (1)..(1290)
<223>

<400> 29

```
atg cag tat gca gaa ctt ctt gac ctc ctg ccc cta caa gaa caa ggg      48
Met Gln Tyr Ala Glu Leu Leu Asp Leu Leu Pro Leu Gln Glu Gln Gly
1               5                   10                  15

aag atg gat ttg ggg cta gca acc atg acc cag gtg atg gac tta ttg      96
Lys Met Asp Leu Gly Leu Ala Thr Met Thr Gln Val Met Asp Leu Leu
                20                  25                  30

ggc aag ccc caa gac cag gtc ccc atg gtt cat atc gct ggc acc aat .    144
Gly Lys Pro Gln Asp Gln Val Pro Met Val His Ile Ala Gly Thr Asn
            35                  40                  45

ggc aag ggg tcg gcc gca gcc ttt aca gag cga ata ctc agg gag gct     192
Gly Lys Gly Ser Ala Ala Ala Phe Thr Glu Arg Ile Leu Arg Glu Ala
        50                  55                  60

ggc tac aag gtc ggc ttg tat att tcc cct tcc cta gtg gaa ttt aat     240
Gly Tyr Lys Val Gly Leu Tyr Ile Ser Pro Ser Leu Val Glu Phe Asn
65                  70                  75                  80

gaa cgg atc caa atc aat ggc caa gcc aca agt gat gat cag ttg ctc     288
Glu Arg Ile Gln Ile Asn Gly Gln Ala Thr Ser Asp Asp Gln Leu Leu
                85                  90                  95

aag gca gtc aag acc cta agc cag gcc tta gaa ggc aca tcc ctt tgc     336
Lys Ala Val Lys Thr Leu Ser Gln Ala Leu Glu Gly Thr Ser Leu Cys
            100                 105                 110

ctg act gaa ttt gaa ctt ttt act gcc ctg gcc ttt ttg acc ttc cag     384
Leu Thr Glu Phe Glu Leu Phe Thr Ala Leu Ala Phe Leu Thr Phe Gln
        115                 120                 125

gac cag gct tgt gat ata gcc gtt gta gag gtc gga tta gga gga cgg     432
Asp Gln Ala Cys Asp Ile Ala Val Val Glu Val Gly Leu Gly Gly Arg
    130                 135                 140

tta gat gct acc aat gtg ata agc cgt cct gcc gtc acc gcc att acc     480
Leu Asp Ala Thr Asn Val Ile Ser Arg Pro Ala Val Thr Ala Ile Thr
145                 150                 155                 160

aag att ggc atg gac cat acc gct ttt tta ggg gat agc ctg cca gaa     528
Lys Ile Gly Met Asp His Thr Ala Phe Leu Gly Asp Ser Leu Pro Glu
                165                 170                 175

ata gcc ggt gag aag gca gcc atc gcc aaa gcc ggc tcg cct atg gtg     576
```

```
Ile Ala Gly Glu Lys Ala Ala Ile Ala Lys Ala Gly Ser Pro Met Val
             180               185               190

gtc tat ccc cag ggg cca gaa gtg act cgg gtg atc caa aat cag gcg    624
Val Tyr Pro Gln Gly Pro Glu Val Thr Arg Val Ile Gln Asn Gln Ala
             195               200               205

gac cgg gta gga gcc tct ctg acc cta att tct caa tcc gac ctg act    672
Asp Arg Val Gly Ala Ser Leu Thr Leu Ile Ser Gln Ser Asp Leu Thr
             210               215               220

tat aac ctg act tcg gac ctc ttg caa gac ttt gaa tac aag cag gtt    720
Tyr Asn Leu Thr Ser Asp Leu Leu Gln Asp Phe Glu Tyr Lys Gln Val
225               230               235               240

ccc tac cgc att tca ctt tta gaa gat tat caa att tac aac gcc ctg    768
Pro Tyr Arg Ile Ser Leu Leu Glu Asp Tyr Gln Ile Tyr Asn Ala Leu
                  245               250               255

gta gca ctc gaa atc tct ttt gcc tta cag gat gct ggc tgg cag att    816
Val Ala Leu Glu Ile Ser Phe Ala Leu Gln Asp Ala Gly Trp Gln Ile
             260               265               270

agc cct aaa gcc att aaa caa ggt ttg gtt gag acc cgc tgg ccc ggc    864
Ser Pro Lys Ala Ile Lys Gln Gly Leu Val Glu Thr Arg Trp Pro Gly
             275               280               285

cgt ttt gaa ctt atc gcc tct cat ccg acc gtg atc gtt gat ggg tct    912
Arg Phe Glu Leu Ile Ala Ser His Pro Thr Val Ile Val Asp Gly Ser
             290               295               300

cat aat gaa gac ggc ctg cag gct ctc ttg gct aac cta gac cgc tac    960
His Asn Glu Asp Gly Leu Gln Ala Leu Leu Ala Asn Leu Asp Arg Tyr
305               310               315               320

ttt cca gaa caa aaa agg att ggg atc gta ggc atg ttg gcc gac aag   1008
Phe Pro Glu Gln Lys Arg Ile Gly Ile Val Gly Met Leu Ala Asp Lys
                  325               330               335

gat gtt gat gcc gcc cta gct cct tta acc aaa agc ttt gac cgg ctt   1056
Asp Val Asp Ala Ala Leu Ala Pro Leu Thr Lys Ser Phe Asp Arg Leu
             340               345               350

tat acg gtg aca ccc gat tcg ccg cgg ggg atg gca gcc cct caa atg   1104
Tyr Thr Val Thr Pro Asp Ser Pro Arg Gly Met Ala Ala Pro Gln Met
             355               360               365

aaa gaa aaa ctg acc gaa atg gtg tcg ccg tct act cgg gtc ata gct   1152
Lys Glu Lys Leu Thr Glu Met Val Ser Pro Ser Thr Arg Val Ile Ala
             370               375               380

tgt gaa agt tat aac cag gcc tta gac ctg gca ggt caa gta gcc ggc   1200
Cys Glu Ser Tyr Asn Gln Ala Leu Asp Leu Ala Gly Gln Val Ala Gly
385               390               395               400

gga gat gac cta att gtc gtt ttt gga agt ttt tat att gtt ggt aag   1248
Gly Asp Asp Leu Ile Val Val Phe Gly Ser Phe Tyr Ile Val Gly Lys
```

```
                    405                    410                    415
ttt aga cag ctg att tta gca aga aga aat ggg gaa gtt taa              1290
Phe Arg Gln Leu Ile Leu Ala Arg Arg Asn Gly Glu Val
            420                    425
```

<210> 30
<211> 429
<212> PRT
<213> Alloiococcus otitidis

<400> 30

```
Met Gln Tyr Ala Glu Leu Leu Asp Leu Leu Pro Leu Gln Glu Gln Gly
1               5                   10                  15


Lys Met Asp Leu Gly Leu Ala Thr Met Thr Gln Val Met Asp Leu Leu
            20                  25                  30


Gly Lys Pro Gln Asp Gln Val Pro Met Val His Ile Ala Gly Thr Asn
            35                  40                  45


Gly Lys Gly Ser Ala Ala Ala Phe Thr Glu Arg Ile Leu Arg Glu Ala
        50                  55                  60


Gly Tyr Lys Val Gly Leu Tyr Ile Ser Pro Ser Leu Val Glu Phe Asn
65                  70                  75                  80


Glu Arg Ile Gln Ile Asn Gly Gln Ala Thr Ser Asp Asp Gln Leu Leu
                85                  90                  95


Lys Ala Val Lys Thr Leu Ser Gln Ala Leu Glu Gly Thr Ser Leu Cys
                100                 105                 110


Leu Thr Glu Phe Glu Leu Phe Thr Ala Leu Ala Phe Leu Thr Phe Gln
        115                 120                 125


Asp Gln Ala Cys Asp Ile Ala Val Val Glu Val Gly Leu Gly Gly Arg
        130                 135                 140


Leu Asp Ala Thr Asn Val Ile Ser Arg Pro Ala Val Thr Ala Ile Thr
145                 150                 155                 160


Lys Ile Gly Met Asp His Thr Ala Phe Leu Gly Asp Ser Leu Pro Glu
                165                 170                 175
```

Ile Ala Gly Glu Lys Ala Ala Ile Ala Lys Ala Gly Ser Pro Met Val
            180   185   190

Val Tyr Pro Gln Gly Pro Glu Val Thr Arg Val Ile Gln Asn Gln Ala
            195   200   205

Asp Arg Val Gly Ala Ser Leu Thr Leu Ile Ser Gln Ser Asp Leu Thr
    210   215   220

Tyr Asn Leu Thr Ser Asp Leu Leu Gln Asp Phe Glu Tyr Lys Gln Val
225   230   235   240

Pro Tyr Arg Ile Ser Leu Leu Glu Asp Tyr Gln Ile Tyr Asn Ala Leu
            245   250   255

Val Ala Leu Glu Ile Ser Phe Ala Leu Gln Asp Ala Gly Trp Gln Ile
            260   265   270

Ser Pro Lys Ala Ile Lys Gln Gly Leu Val Glu Thr Arg Trp Pro Gly
            275   280   285

Arg Phe Glu Leu Ile Ala Ser His Pro Thr Val Ile Val Asp Gly Ser
    290   295   300

His Asn Glu Asp Gly Leu Gln Ala Leu Leu Ala Asn Leu Asp Arg Tyr
305   310   315   320

Phe Pro Glu Gln Lys Arg Ile Gly Ile Val Gly Met Leu Ala Asp Lys
            325   330   335

Asp Val Asp Ala Ala Leu Ala Pro Leu Thr Lys Ser Phe Asp Arg Leu
            340   345   350

Tyr Thr Val Thr Pro Asp Ser Pro Arg Gly Met Ala Ala Pro Gln Met
            355   360   365

Lys Glu Lys Leu Thr Glu Met Val Ser Pro Ser Thr Arg Val Ile Ala
    370   375   380

Cys Glu Ser Tyr Asn Gln Ala Leu Asp Leu Ala Gly Gln Val Ala Gly
385   390   395   400

Gly Asp Asp Leu Ile Val Val Phe Gly Ser Phe Tyr Ile Val Gly Lys

```
                    405                   410                   415


        Phe Arg Gln Leu Ile Leu Ala Arg Arg Asn Gly Glu Val
                 420                 425



<210> 31
<211> 387
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (16)..(387)
<223>


<400> 31
agaaagagga ataag atg gat aaa aga gat aag ata cgc ttg caa ggg atg        51
               Met Asp Lys Arg Asp Lys Ile Arg Leu Gln Gly Met
                1             5                   10


act ttt cac ggc cac cac ggt ttg atg gag gcc gaa acc aag ttg ggt        99
Thr Phe His Gly His His Gly Leu Met Glu Ala Glu Thr Lys Leu Gly
         15                 20                  25


cag att ttt aaa gtc gac ctt gtc tta gta act gac ctc aag tta gcg       147
Gln Ile Phe Lys Val Asp Leu Val Leu Val Thr Asp Leu Lys Leu Ala
     30                  35                  40


ggt caa aca gac aag atg ggg cac agt atc cac tac ggg gaa gtt tat       195
Gly Gln Thr Asp Lys Met Gly His Ser Ile His Tyr Gly Glu Val Tyr
45                  50                  55                  60


gac ctg gtc aag tcc att gtg gaa ggt acc ccc ttt aag ctt ttg gag       243
Asp Leu Val Lys Ser Ile Val Glu Gly Thr Pro Phe Lys Leu Leu Glu
                65                  70                  75


tcc ttg gcg gaa acc cta gcc caa gaa gtt ctc aag act ttt gac cag       291
Ser Leu Ala Glu Thr Leu Ala Gln Glu Val Leu Lys Thr Phe Asp Gln
             80                  85                  90


gtt gag gag gtc ttg gtc cgg gtc aac aaa ccc cag gcc ccg att cct       339
Val Glu Glu Val Leu Val Arg Val Asn Lys Pro Gln Ala Pro Ile Pro
             95                 100                 105


ggt gtc ttt gac aat gta gcg gtg gaa atc acc cgg gcc cgt cac tag       387
Gly Val Phe Asp Asn Val Ala Val Glu Ile Thr Arg Ala Arg His
         110                 115                 120


<210> 32
<211> 123
<212> PRT
<213> Alloiococcus otitidis

<400> 32
```

```
Met Asp Lys Arg Asp Lys Ile Arg Leu Gln Gly Met Thr Phe His Gly
1               5               10              15

His His Gly Leu Met Glu Ala Glu Thr Lys Leu Gly Gln Ile Phe Lys
            20              25              30

Val Asp Leu Val Leu Val Thr Asp Leu Lys Leu Ala Gly Gln Thr Asp
        35              40              45

Lys Met Gly His Ser Ile His Tyr Gly Glu Val Tyr Asp Leu Val Lys
    50              55              60

Ser Ile Val Glu Gly Thr Pro Phe Lys Leu Leu Glu Ser Leu Ala Glu
65              70              75              80

Thr Leu Ala Gln Glu Val Leu Lys Thr Phe Asp Gln Val Glu Glu Val
            85              90              95

Leu Val Arg Val Asn Lys Pro Gln Ala Pro Ile Pro Gly Val Phe Asp
            100             105             110

Asn Val Ala Val Glu Ile Thr Arg Ala Arg His
        115             120
```

```
<210> 33
<211> 552
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (22)..(552)
<223>

<400> 33
ataggtaagg aggaatatag a gtg aag ggt gtt atg ata gga ctc ggt tct      51
                       Met Lys Gly Val Met Ile Gly Leu Gly Ser
                       1               5               10

aat atg ggg act aag ttg gct tac tta aac cgg gct ttg gcc aaa ata      99
Asn Met Gly Thr Lys Leu Ala Tyr Leu Asn Arg Ala Leu Ala Lys Ile
            15              20              25

aat agc cta gac cag gta gca gtc aag caa gtt tca aag gtt tac cag     147
Asn Ser Leu Asp Gln Val Ala Val Lys Gln Val Ser Lys Val Tyr Gln
            30              35              40

act gaa ccg gtg ggc tac aag gac cag gac gat ttt tac aat atg gtt     195
Thr Glu Pro Val Gly Tyr Lys Asp Gln Asp Asp Phe Tyr Asn Met Val
```

```
              45                      50                      55
gct ggc ctt gaa att gaa cca ggc aag acc ccc ttg gac ctc tta gaa      243
Ala Gly Leu Glu Ile Glu Pro Gly Lys Thr Pro Leu Asp Leu Leu Glu
         60                      65                      70

gac ttg ctg gcg att gag gca gac ctg gac agg aag cgg acc att aaa      291
Asp Leu Leu Ala Ile Glu Ala Asp Leu Asp Arg Lys Arg Thr Ile Lys
75                       80                      85                      90

aat ggc ccc cga acc att gac ttg gat gtc ttg ctg gtg gag ggt caa      339
Asn Gly Pro Arg Thr Ile Asp Leu Asp Val Leu Leu Val Glu Gly Gln
                    95                      100                     105

gaa att gac cat ccc aag ctc caa gtt ccc cac cca agg ctc cag gac      387
Glu Ile Asp His Pro Lys Leu Gln Val Pro His Pro Arg Leu Gln Asp
                   110                      115                     120

cgg gcc ttt gtc ttg gtc ccc ttg gct gag ttg gac ccc aac tac ctg      435
Arg Ala Phe Val Leu Val Pro Leu Ala Glu Leu Asp Pro Asn Tyr Leu
                   125                      130                     135

gtt cct ggc ata gat aag aca gtt gcg gac ttg ttg gct tct tta aac      483
Val Pro Gly Ile Asp Lys Thr Val Ala Asp Leu Leu Ala Ser Leu Asn
         140                      145                     150

caa acc gac cta gca ggg gtg gag gct ttg ggt cag ttg acg aac cta      531
Gln Thr Asp Leu Ala Gly Val Glu Ala Leu Gly Gln Leu Thr Asn Leu
155                      160                     165                     170

tta gaa gac cgt gag gct tga                                          552
Leu Glu Asp Arg Glu Ala
                   175
```

<210> 34
<211> 176
<212> PRT
<213> Alloiococcus otitidis

<400> 34
```
Met Lys Gly Val Met Ile Gly Leu Gly Ser Asn Met Gly Thr Lys Leu
1                 5                   10                  15

Ala Tyr Leu Asn Arg Ala Leu Ala Lys Ile Asn Ser Leu Asp Gln Val
                20                  25                  30

Ala Val Lys Gln Val Ser Lys Val Tyr Gln Thr Glu Pro Val Gly Tyr
           35                  40                  45

Lys Asp Gln Asp Asp Phe Tyr Asn Met Val Ala Gly Leu Glu Ile Glu
         50                  55                  60
```

```
Pro Gly Lys Thr Pro Leu Asp Leu Leu Glu Asp Leu Leu Ala Ile Glu
65              70              75              80


Ala Asp Leu Asp Arg Lys Arg Thr Ile Lys Asn Gly Pro Arg Thr Ile
                85              90              95


Asp Leu Asp Val Leu Leu Val Glu Gly Gln Glu Ile Asp His Pro Lys
            100             105             110


Leu Gln Val Pro His Pro Arg Leu Gln Asp Arg Ala Phe Val Leu Val
        115             120             125


Pro Leu Ala Glu Leu Asp Pro Asn Tyr Leu Val Pro Gly Ile Asp Lys
    130             135             140


Thr Val Ala Asp Leu Leu Ala Ser Leu Asn Gln Thr Asp Leu Ala Gly
145             150             155             160


Val Glu Ala Leu Gly Gln Leu Thr Asn Leu Leu Glu Asp Arg Glu Ala
                165             170             175
```

```
<210> 35
<211> 1242
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (40)..(1242)
<223>

<400> 35
aatcttctta atatcgcttg gcccaagacc gctataata gtg gta agt gat tat        54
                                            Met Val Ser Asp Tyr
                                            1               5

ttt agg agg ttc aat atg caa ata gga att gac aag ctg gct ttt gcg    102
Phe Arg Arg Phe Asn Met Gln Ile Gly Ile Asp Lys Leu Ala Phe Ala
            10              15                  20

act cca acc agg tac ttg gaa atg gcg agt ctg gcc caa gcc cgg tcc    150
Thr Pro Thr Arg Tyr Leu Glu Met Ala Ser Leu Ala Gln Ala Arg Ser
        25              30                  35

caa gac cct aat aaa tat atc aag ggg cta ggc caa gaa gcc atg gct    198
Gln Asp Pro Asn Lys Tyr Ile Lys Gly Leu Gly Gln Glu Ala Met Ala
        40              45                  50
```

```
gtc cct gaa gaa agt gat gat gcc gtc agc ttg gcg gct aat gcc ggt      246
Val Pro Glu Glu Ser Asp Asp Ala Val Ser Leu Ala Ala Asn Ala Gly
    55              60              65

aat tta atc tta agt gaa gaa gac aag gct gct att gac atg gtg ata      294
Asn Leu Ile Leu Ser Glu Glu Asp Lys Ala Ala Ile Asp Met Val Ile
70              75              80              85

gtc ggt acc gaa tct ggg gtc gac cag tcc aag tcg gca gcc agc tgg      342
Val Gly Thr Glu Ser Gly Val Asp Gln Ser Lys Ser Ala Ala Ser Trp
            90              95              100

gtt cat gac ctg ttg ggg atc aac ccc cat gct aga agc ctg gag atc      390
Val His Asp Leu Leu Gly Ile Asn Pro His Ala Arg Ser Leu Glu Ile
            105             110             115

aag caa gcc tgc tac ggg gct acg gct gga ctc aaa cta gct gtg gcc      438
Lys Gln Ala Cys Tyr Gly Ala Thr Ala Gly Leu Lys Leu Ala Val Ala
        120             125             130

cac cta gcc tta aac cct gac tcc aag gtt tta gtc atc ggt tca gac      486
His Leu Ala Leu Asn Pro Asp Ser Lys Val Leu Val Ile Gly Ser Asp
    135             140             145

ata gcc aag tat ggt ttg gaa aca ggg ggc gag ccc act caa gga gct      534
Ile Ala Lys Tyr Gly Leu Glu Thr Gly Gly Glu Pro Thr Gln Gly Ala
150             155             160             165

ggg gcg gtc gcc atc tta gtc agc cgt gac cct gca att gct gtg gtc      582
Gly Ala Val Ala Ile Leu Val Ser Arg Asp Pro Ala Ile Ala Val Val
            170             175             180

aac aat gac agt gcc atg ctg acc aaa aat att gca gac ttt tgg cga      630
Asn Asn Asp Ser Ala Met Leu Thr Lys Asn Ile Ala Asp Phe Trp Arg
            185             190             195

ccc aac tac agc gat tat gcc cat gta gat ggc aag ttc tcc aac cag      678
Pro Asn Tyr Ser Asp Tyr Ala His Val Asp Gly Lys Phe Ser Asn Gln
        200             205             210

gca tac ttg tcc aac cta gca gaa gtc tgg cgc cag tat aag atc aaa      726
Ala Tyr Leu Ser Asn Leu Ala Glu Val Trp Arg Gln Tyr Lys Ile Lys
    215             220             225

aac cag ctg tct gct aag gat ttc aag gcc atg gtc ttc cac agc ccc      774
Asn Gln Leu Ser Ala Lys Asp Phe Lys Ala Met Val Phe His Ser Pro
230             235             240             245

tat acc aag atg ggg aaa aag gcc tta ctc aaa cta gga gat tat gaa      822
Tyr Thr Lys Met Gly Lys Lys Ala Leu Leu Lys Leu Gly Asp Tyr Glu
            250             255             260

gac cag aaa gag att gac cgc ttg ctg gcc tat tac gag cct ggt cgc      870
Asp Gln Lys Glu Ile Asp Arg Leu Leu Ala Tyr Tyr Glu Pro Gly Arg
            265             270             275
```

```
tac tac aat aag cgg gtc ggt aat atc tat act ggg tct ctt tac ttg      918
Tyr Tyr Asn Lys Arg Val Gly Asn Ile Tyr Thr Gly Ser Leu Tyr Leu
        280             285             290

agt ttg att tcc ctc tta gac cag gta agt gac ctg gag gct ggc gac      966
Ser Leu Ile Ser Leu Leu Asp Gln Val Ser Asp Leu Glu Ala Gly Asp
        295             300             305

cgg att ggc ctc tat tct tat ggg tct ggt gcc gtt gga gag ttc ttt     1014
Arg Ile Gly Leu Tyr Ser Tyr Gly Ser Gly Ala Val Gly Glu Phe Phe
310             315             320             325

agc att cgg ctc cag cca ggt tac aag gaa agc tta cag caa gtt gac     1062
Ser Ile Arg Leu Gln Pro Gly Tyr Lys Glu Ser Leu Gln Gln Val Asp
            330             335             340

ttc gac cag gtt gtc aac cag cgt tca gca tta gag atg tac agc tat     1110
Phe Asp Gln Val Val Asn Gln Arg Ser Ala Leu Glu Met Tyr Ser Tyr
            345             350             355

cag gac ttg ctg acc ttt agc cta cct caa gac ggc caa act tac act     1158
Gln Asp Leu Leu Thr Phe Ser Leu Pro Gln Asp Gly Gln Thr Tyr Thr
            360             365             370

aca gat aaa agt cac cag gtc cca ggc cgt ttt gtc tta gac cgg gtg     1206
Thr Asp Lys Ser His Gln Val Pro Gly Arg Phe Val Leu Asp Arg Val
        375             380             385

gcc gac cat atc cgt tac tac cgg cgc ttg gct taa                     1242
Ala Asp His Ile Arg Tyr Tyr Arg Arg Leu Ala
390             395             400


<210> 36
<211> 400
<212> PRT
<213> Alloiococcus otitidis

<400> 36
Met Val Ser Asp Tyr Phe Arg Arg Phe Asn Met Gln Ile Gly Ile Asp
1               5               10              15


Lys Leu Ala Phe Ala Thr Pro Thr Arg Tyr Leu Glu Met Ala Ser Leu
            20              25              30


Ala Gln Ala Arg Ser Gln Asp Pro Asn Lys Tyr Ile Lys Gly Leu Gly
            35              40              45


Gln Glu Ala Met Ala Val Pro Glu Glu Ser Asp Asp Ala Val Ser Leu
        50              55              60


Ala Ala Asn Ala Gly Asn Leu Ile Leu Ser Glu Glu Asp Lys Ala Ala
65              70              75              80
```

```
Ile Asp Met Val Ile Val Gly Thr Glu Ser Gly Val Asp Gln Ser Lys
                  85              90              95

Ser Ala Ala Ser Trp Val His Asp Leu Leu Gly Ile Asn Pro His Ala
             100              105              110

Arg Ser Leu Glu Ile Lys Gln Ala Cys Tyr Gly Ala Thr Ala Gly Leu
         115              120              125

Lys Leu Ala Val Ala His Leu Ala Leu Asn Pro Asp Ser Lys Val Leu
     130              135              140

Val Ile Gly Ser Asp Ile Ala Lys Tyr Gly Leu Glu Thr Gly Gly Glu
145              150              155              160

Pro Thr Gln Gly Ala Gly Ala Val Ala Ile Leu Val Ser Arg Asp Pro
                 165              170              175

Ala Ile Ala Val Val Asn Asn Asp Ser Ala Met Leu Thr Lys Asn Ile
             180              185              190

Ala Asp Phe Trp Arg Pro Asn Tyr Ser Asp Tyr Ala His Val Asp Gly
         195              200              205

Lys Phe Ser Asn Gln Ala Tyr Leu Ser Asn Leu Ala Glu Val Trp Arg
     210              215              220

Gln Tyr Lys Ile Lys Asn Gln Leu Ser Ala Lys Asp Phe Lys Ala Met
225              230              235              240

Val Phe His Ser Pro Tyr Thr Lys Met Gly Lys Lys Ala Leu Leu Lys
                 245              250              255

Leu Gly Asp Tyr Glu Asp Gln Lys Glu Ile Asp Arg Leu Leu Ala Tyr
             260              265              270

Tyr Glu Pro Gly Arg Tyr Tyr Asn Lys Arg Val Gly Asn Ile Tyr Thr
         275              280              285

Gly Ser Leu Tyr Leu Ser Leu Ile Ser Leu Leu Asp Gln Val Ser Asp
     290              295              300
```

```
Leu Glu Ala Gly Asp Arg Ile Gly Leu Tyr Ser Tyr Gly Ser Gly Ala
305                 310             315                 320


Val Gly Glu Phe Phe Ser Ile Arg Leu Gln Pro Gly Tyr Lys Glu Ser
                325                 330                 335


Leu Gln Gln Val Asp Phe Asp Gln Val Val Asn Gln Arg Ser Ala Leu
            340                 345                 350


Glu Met Tyr Ser Tyr Gln Asp Leu Leu Thr Phe Ser Leu Pro Gln Asp
        355                 360             365


Gly Gln Thr Tyr Thr Thr Asp Lys Ser His Gln Val Pro Gly Arg Phe
    370                 375                 380


Val Leu Asp Arg Val Ala Asp His Ile Arg Tyr Tyr Arg Arg Leu Ala
385                 390                 395                 400
```

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<210> 37
<211> 1323
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (31)..(1323)
<223>

<400> 37
 ttctggtata gattaaggaa ggaggagacc atg tta ccc tta ttc aag caa ttt        54
                                     Met Leu Pro Leu Phe Lys Gln Phe
                                     1                5

 tac aag caa agc ctc agc cag cgc ctc aaa gct cta gaa aag gcc ggc        102
 Tyr Lys Gln Ser Leu Ser Gln Arg Leu Lys Ala Leu Glu Lys Ala Gly
     10              15                  20

 tat ctt gat cct gac cag gcg ggt aaa ctc cag tca ggg gaa ctg ggt        150
 Tyr Leu Asp Pro Asp Gln Ala Gly Lys Leu Gln Ser Gly Glu Leu Gly
 25              30                  35                  40

 ttg acc cat gaa gcc ggc gac cac atg att gaa aac tac atc ggc tcc        198
 Leu Thr His Glu Ala Gly Asp His Met Ile Glu Asn Tyr Ile Gly Ser
                 45                  50                  55

 tat acc ctc cct ctg gga ctg gcc ctc cac ttt tta ctc gat ggc aag        246
 Tyr Thr Leu Pro Leu Gly Leu Ala Leu His Phe Leu Leu Asp Gly Lys
```

```
                    60                    65                    70
agc tac cta gtc ccc atg gct att gaa gag ccc tct gtc att gcc gct        294
Ser Tyr Leu Val Pro Met Ala Ile Glu Glu Pro Ser Val Ile Ala Ala
        75                    80                    85

gcc agc aac ggt gcc aag atg gta gcc caa agc ggt ggt ttc cat aca        342
Ala Ser Asn Gly Ala Lys Met Val Ala Gln Ser Gly Gly Phe His Thr
        90                    95                   100

gtc aag gaa aac cgg ctg atg atc ggt caa gtg gtc ata gcc gga agc        390
Val Lys Glu Asn Arg Leu Met Ile Gly Gln Val Val Ile Ala Gly Ser
105                   110                   115                   120

aca aaa cct agc cag gac cgg gga aaa atc ctg agc cac cag caa gac        438
Thr Lys Pro Ser Gln Asp Arg Gly Lys Ile Leu Ser His Gln Gln Asp
                    125                   130                   135

tta atc gac cta gcc aat gct agc tat ccc tca att ggt aaa aga ggg        486
Leu Ile Asp Leu Ala Asn Ala Ser Tyr Pro Ser Ile Gly Lys Arg Gly
                    140                   145                   150

ggt ggg gcc cga ggc att caa gtc aaa cag ttt gac tca gac ctg ggc        534
Gly Gly Ala Arg Gly Ile Gln Val Lys Gln Phe Asp Ser Asp Leu Gly
                    155                   160                   165

cag gat atg gga agc tat ctg gca gtc tac ttg act gtt gac tgc cag        582
Gln Asp Met Gly Ser Tyr Leu Ala Val Tyr Leu Thr Val Asp Cys Gln
        170                   175                   180

gaa gcc atg ggg gct aac att atc aac acc atg ctg gaa gcc ctg gct        630
Glu Ala Met Gly Ala Asn Ile Ile Asn Thr Met Leu Glu Ala Leu Ala
185                   190                   195                   200

cct gaa att gac cgc cta acc agc ggc cag gtc ttg atg tcc atc tta        678
Pro Glu Ile Asp Arg Leu Thr Ser Gly Gln Val Leu Met Ser Ile Leu
                    205                   210                   215

tct aac ctg gcc act gaa tcc ctt gtc act gtt tcc tgt caa gta aaa        726
Ser Asn Leu Ala Thr Glu Ser Leu Val Thr Val Ser Cys Gln Val Lys
                    220                   225                   230

ccc aga ttt tta gtc aaa aat gac atg gca ggg gaa gct gtc cgg gac        774
Pro Arg Phe Leu Val Lys Asn Asp Met Ala Gly Glu Ala Val Arg Asp
                    235                   240                   245

caa atc atc cag gcc tac cag tat gcc tgc ctg gac ccc tac cgg gca        822
Gln Ile Ile Gln Ala Tyr Gln Tyr Ala Cys Leu Asp Pro Tyr Arg Ala
        250                   255                   260

gcc acc cac aac aag ggg atc atg aac ggg gta gac ggc ttg gtc cta        870
Ala Thr His Asn Lys Gly Ile Met Asn Gly Val Asp Gly Leu Val Leu
265                   270                   275                   280

gct agt ggg aat gat tgg cgg gca atc gaa gcg ggg gcc cat gct tac        918
Ala Ser Gly Asn Asp Trp Arg Ala Ile Glu Ala Gly Ala His Ala Tyr
                    285                   290                   295
```

```
gct agt ttg acc ggc cac tac cgc ccc ttg tcc aag tgg gaa aag acc    966
Ala Ser Leu Thr Gly His Tyr Arg Pro Leu Ser Lys Trp Glu Lys Thr
            300                 305                 310

caa gac gga cag tta aaa ggg acc att acc ctt ccc ttg cca att gcc   1014
Gln Asp Gly Gln Leu Lys Gly Thr Ile Thr Leu Pro Leu Pro Ile Ala
            315                 320                 325

aca gtt ggt ggg gct att gcc tcc cac cct gta gcc caa gtt agc cag   1062
Thr Val Gly Gly Ala Ile Ala Ser His Pro Val Ala Gln Val Ser Gln
            330                 335                 340

caa atc tta ggc caa cct act gct aag caa tta gcc cgg ctg gtt gca   1110
Gln Ile Leu Gly Gln Pro Thr Ala Lys Gln Leu Ala Arg Leu Val Ala
345                 350                 355                 360

gca gtg gga cta gcc cag aac cta tcc gct ctt cgt gcc tta gtc aca   1158
Ala Val Gly Leu Ala Gln Asn Leu Ser Ala Leu Arg Ala Leu Val Thr
            365                 370                 375

act ggt att caa caa gga cac atg gcc ctc cag gca agg tct ttg gcc   1206
Thr Gly Ile Gln Gln Gly His Met Ala Leu Gln Ala Arg Ser Leu Ala
            380                 385                 390

atg aat gcc ggg gcc cgg gga gac aag atc caa aag ctg gca gac cgc   1254
Met Asn Ala Gly Ala Arg Gly Asp Lys Ile Gln Lys Leu Ala Asp Arg
            395                 400                 405

tta att aac caa gac caa atg aac cta gca act gcc cgt gcc ctg ctc   1302
Leu Ile Asn Gln Asp Gln Met Asn Leu Ala Thr Ala Arg Ala Leu Leu
            410                 415                 420

aag aac atg gaa gaa gac taa                                        1323
Lys Asn Met Glu Glu Asp
425                 430
```

```
<210> 38
<211> 430
<212> PRT
<213> Alloiococcus otitidis

<400> 38
Met Leu Pro Leu Phe Lys Gln Phe Tyr Lys Gln Ser Leu Ser Gln Arg
1               5                   10                  15


Leu Lys Ala Leu Glu Lys Ala Gly Tyr Leu Asp Pro Asp Gln Ala Gly
            20                  25                  30


Lys Leu Gln Ser Gly Glu Leu Gly Leu Thr His Glu Ala Gly Asp His
            35                  40                  45


Met Ile Glu Asn Tyr Ile Gly Ser Tyr Thr Leu Pro Leu Gly Leu Ala
```

```
         50                    55                    60

Leu His Phe Leu Leu Asp Gly Lys Ser Tyr Leu Val Pro Met Ala Ile
65              70              75              80

Glu Glu Pro Ser Val Ile Ala Ala Ala Ser Asn Gly Ala Lys Met Val
            85              90              95

Ala Gln Ser Gly Gly Phe His Thr Val Lys Glu Asn Arg Leu Met Ile
        100             105             110

Gly Gln Val Val Ile Ala Gly Ser Thr Lys Pro Ser Gln Asp Arg Gly
        115             120             125

Lys Ile Leu Ser His Gln Gln Asp Leu Ile Asp Leu Ala Asn Ala Ser
    130             135             140

Tyr Pro Ser Ile Gly Lys Arg Gly Gly Gly Ala Arg Gly Ile Gln Val
145             150             155             160

Lys Gln Phe Asp Ser Asp Leu Gly Gln Asp Met Gly Ser Tyr Leu Ala
            165             170             175

Val Tyr Leu Thr Val Asp Cys Gln Glu Ala Met Gly Ala Asn Ile Ile
            180             185             190

Asn Thr Met Leu Glu Ala Leu Ala Pro Glu Ile Asp Arg Leu Thr Ser
        195             200             205

Gly Gln Val Leu Met Ser Ile Leu Ser Asn Leu Ala Thr Glu Ser Leu
    210             215             220

Val Thr Val Ser Cys Gln Val Lys Pro Arg Phe Leu Val Lys Asn Asp
225             230             235             240

Met Ala Gly Glu Ala Val Arg Asp Gln Ile Ile Gln Ala Tyr Gln Tyr
            245             250             255

Ala Cys Leu Asp Pro Tyr Arg Ala Ala Thr His Asn Lys Gly Ile Met
            260             265             270

Asn Gly Val Asp Gly Leu Val Leu Ala Ser Gly Asn Asp Trp Arg Ala
    275             280             285
```

```
Ile Glu Ala Gly Ala His Ala Tyr Ala Ser Leu Thr Gly His Tyr Arg
    290                 295                 300

Pro Leu Ser Lys Trp Glu Lys Thr Gln Asp Gly Gln Leu Lys Gly Thr
305                 310                 315                 320

Ile Thr Leu Pro Leu Pro Ile Ala Thr Val Gly Gly Ala Ile Ala Ser
                325                 330                 335

His Pro Val Ala Gln Val Ser Gln Gln Ile Leu Gly Gln Pro Thr Ala
                340                 345                 350

Lys Gln Leu Ala Arg Leu Val Ala Ala Val Gly Leu Ala Gln Asn Leu
        355                 360                 365

Ser Ala Leu Arg Ala Leu Val Thr Thr Gly Ile Gln Gln Gly His Met
    370                 375                 380

Ala Leu Gln Ala Arg Ser Leu Ala Met Asn Ala Gly Ala Arg Gly Asp
385                 390                 395                 400

Lys Ile Gln Lys Leu Ala Asp Arg Leu Ile Asn Gln Asp Gln Met Asn
                405                 410                 415

Leu Ala Thr Ala Arg Ala Leu Leu Lys Asn Met Glu Glu Asp
                420                 425                 430
```

```
<210> 39
<211> 930
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (13)..(930)
<223>

<400> 39
aggattagta aa atg tta ttt gat cgt atc gta gaa gcc ttt ccc gaa agc     51
           Met Leu Phe Asp Arg Ile Val Glu Ala Phe Pro Glu Ser
            1               5                   10

aac atc aaa aaa gat gaa ccc ttg tcc tat tac tct tac act cga aca        99
Asn Ile Lys Lys Asp Glu Pro Leu Ser Tyr Tyr Ser Tyr Thr Arg Thr
 15                  20                  25
```

```
ggt ggc ccg gct gac att ttg att ttc cca gaa tcc atc gat gaa att          147
Gly Gly Pro Ala Asp Ile Leu Ile Phe Pro Glu Ser Ile Asp Glu Ile
30                  35                  40                  45

gtg acg att atc aag tgg atc aac caa agt ccg gaa tac caa gct ggc          195
Val Thr Ile Ile Lys Trp Ile Asn Gln Ser Pro Glu Tyr Gln Ala Gly
                50                  55                  60

gat ctc ccc ctc act atc tta ggc aat gct agc aac ctg atc gta aaa          243
Asp Leu Pro Leu Thr Ile Leu Gly Asn Ala Ser Asn Leu Ile Val Lys
                65                  70                  75

gat ggt ggg ata aga ggg att acc atc att acc acc ggc att aaa acc          291
Asp Gly Gly Ile Arg Gly Ile Thr Ile Ile Thr Thr Gly Ile Lys Thr
            80                  85                  90

att tgt cac gaa gag aac cgg atc act gcg ggc gct gga gca gct att          339
Ile Cys His Glu Glu Asn Arg Ile Thr Ala Gly Ala Gly Ala Ala Ile
    95                  100                 105

atc gat gtt agc cag gct gcc ttg gac cat agc tta act ggc ttg gaa          387
Ile Asp Val Ser Gln Ala Ala Leu Asp His Ser Leu Thr Gly Leu Glu
110                 115                 120                 125

ttc gct tgt ggc ata ccg ggt agt aca ggc ggg gct gtt tac atg aac          435
Phe Ala Cys Gly Ile Pro Gly Ser Thr Gly Gly Ala Val Tyr Met Asn
                130                 135                 140

gct ggg gct tac ggt ggg gaa gtc cag cat tgt gtt gaa agt gtc caa          483
Ala Gly Ala Tyr Gly Gly Glu Val Gln His Cys Val Glu Ser Val Gln
            145                 150                 155

gtc ttg acc cgg cat ggc cag ttg aag acc tat agt aat gcg gaa atg          531
Val Leu Thr Arg His Gly Gln Leu Lys Thr Tyr Ser Asn Ala Glu Met
            160                 165                 170

aac ttc tcc tac cgc cac agt tat ttg atg gaa gaa gac gat ata gta          579
Asn Phe Ser Tyr Arg His Ser Tyr Leu Met Glu Glu Asp Asp Ile Val
        175                 180                 185

gtc tcc gtg acc ttt aaa ttg gag tcg ggc gac tac atc act atc aag          627
Val Ser Val Thr Phe Lys Leu Glu Ser Gly Asp Tyr Ile Thr Ile Lys
190                 195                 200                 205

gaa aag atg gat gaa tta acc tac ctt aga gaa tcc aaa caa ccg ctg          675
Glu Lys Met Asp Glu Leu Thr Tyr Leu Arg Glu Ser Lys Gln Pro Leu
                210                 215                 220

gaa tac ccc tct tgt ggg tca gtc ttt aaa aga cct gaa ggc cac ttt          723
Glu Tyr Pro Ser Cys Gly Ser Val Phe Lys Arg Pro Glu Gly His Phe
                225                 230                 235

acg ggg aaa tta atc cag gat gct ggc ctt caa gga ttg gtc cat ggt          771
Thr Gly Lys Leu Ile Gln Asp Ala Gly Leu Gln Gly Leu Val His Gly
            240                 245                 250

gga gcc cag gta tcc gaa aaa cat gcc ggt ttt atc att aat ata ggc          819
```

```
Gly Ala Gln Val Ser Glu Lys His Ala Gly Phe Ile Ile Asn Ile Gly
    255                 260             265

aat gct acc gcc agc gac tac caa gag ttg atc caa cat atc caa gaa      867
Asn Ala Thr Ala Ser Asp Tyr Gln Glu Leu Ile Gln His Ile Gln Glu
270                 275             280             285

gaa gtc tac cgg att tac aag gtt aag ctg gaa cgt gaa gtt cgc att      915
Glu Val Tyr Arg Ile Tyr Lys Val Lys Leu Glu Arg Glu Val Arg Ile
                290             295             300

ata ggg gag gat tag                                                  930
Ile Gly Glu Asp
            305
```

```
<210> 40
<211> 305
<212> PRT
<213> Alloiococcus otitidis

<400> 40
Met Leu Phe Asp Arg Ile Val Glu Ala Phe Pro Glu Ser Asn Ile Lys
1               5               10              15


Lys Asp Glu Pro Leu Ser Tyr Tyr Ser Tyr Thr Arg Thr Gly Gly Pro
            20              25              30


Ala Asp Ile Leu Ile Phe Pro Glu Ser Ile Asp Glu Ile Val Thr Ile
        35              40              45


Ile Lys Trp Ile Asn Gln Ser Pro Glu Tyr Gln Ala Gly Asp Leu Pro
    50              55              60


Leu Thr Ile Leu Gly Asn Ala Ser Asn Leu Ile Val Lys Asp Gly Gly
65              70              75              80


Ile Arg Gly Ile Thr Ile Ile Thr Thr Gly Ile Lys Thr Ile Cys His
                85              90              95


Glu Glu Asn Arg Ile Thr Ala Gly Ala Gly Ala Ala Ile Ile Asp Val
            100             105             110


Ser Gln Ala Ala Leu Asp His Ser Leu Thr Gly Leu Glu Phe Ala Cys
        115             120             125


Gly Ile Pro Gly Ser Thr Gly Gly Ala Val Tyr Met Asn Ala Gly Ala
    130             135             140
```

```
Tyr Gly Gly Glu Val Gln His Cys Val Glu Ser Val Gln Val Leu Thr
145             150             155             160

Arg His Gly Gln Leu Lys Thr Tyr Ser Asn Ala Glu Met Asn Phe Ser
            165             170             175

Tyr Arg His Ser Tyr Leu Met Glu Glu Asp Asp Ile Val Val Ser Val
            180             185             190

Thr Phe Lys Leu Glu Ser Gly Asp Tyr Ile Thr Ile Lys Glu Lys Met
            195             200             205

Asp Glu Leu Thr Tyr Leu Arg Glu Ser Lys Gln Pro Leu Glu Tyr Pro
    210             215             220

Ser Cys Gly Ser Val Phe Lys Arg Pro Glu Gly His Phe Thr Gly Lys
225             230             235             240

Leu Ile Gln Asp Ala Gly Leu Gln Gly Leu Val His Gly Gly Ala Gln
            245             250             255

Val Ser Glu Lys His Ala Gly Phe Ile Ile Asn Ile Gly Asn Ala Thr
            260             265             270

Ala Ser Asp Tyr Gln Glu Leu Ile Gln His Ile Gln Glu Glu Val Tyr
    275             280             285

Arg Ile Tyr Lys Val Lys Leu Glu Arg Glu Val Arg Ile Ile Gly Glu
    290             295             300

Asp
305
```

```
<210> 41
<211> 1104
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (16)..(1104)
<223>

<400> 41
aaagctggtg ttttc atg gtt tat agc tta agg att ccg ggg aaa ctt tat        51
```

```
                    Met Val Tyr Ser Leu Arg Ile Pro Gly Lys Leu Tyr
                    1               5               10

ttg gca ggt gaa tac gca gta gta acc ccc ggc tat gcc ggg atc ttg          99
Leu Ala Gly Glu Tyr Ala Val Val Thr Pro Gly Tyr Ala Gly Ile Leu
        15              20              25

ctg aca gtc agc cgg tat ttg act tta gac att tgg gaa aca tct ccc         147
Leu Thr Val Ser Arg Tyr Leu Thr Leu Asp Ile Trp Glu Thr Ser Pro
        30              35              40

gac caa gct tca gtc agg tct caa aca tat ggc aac cag gcc tat gct         195
Asp Gln Ala Ser Val Arg Ser Gln Thr Tyr Gly Asn Gln Ala Tyr Ala
45              50              55              60

tgg gag cgg tta gat ggt atc ttt agc ttt aag gac tgg tcc cac ccc         243
Trp Glu Arg Leu Asp Gly Ile Phe Ser Phe Lys Asp Trp Ser His Pro
                65              70              75

ttc cac cta gtc gaa acg gtg atc caa aca gtg gaa gcc tac ata gaa         291
Phe His Leu Val Glu Thr Val Ile Gln Thr Val Glu Ala Tyr Ile Glu
                80              85              90

tcc ttg tcc ctg cct tta aaa agt tac ggg att cag atc aag agc cag         339
Ser Leu Ser Leu Pro Leu Lys Ser Tyr Gly Ile Gln Ile Lys Ser Gln
        95              100             105

ttg gac tac cag ggc aaa aaa att ggc ctg ggg tct agt ggg gcc gtt         387
Leu Asp Tyr Gln Gly Lys Lys Ile Gly Leu Gly Ser Ser Gly Ala Val
        110             115             120

acc atc gct gtt atc cga ggc ctg agc ctt ctt tac gac ctc cac tta         435
Thr Ile Ala Val Ile Arg Gly Leu Ser Leu Leu Tyr Asp Leu His Leu
125             130             135             140

aaa gac ata gac att ttc aaa cta gct gcc atc gcc cat atc cag cta         483
Lys Asp Ile Asp Ile Phe Lys Leu Ala Ala Ile Ala His Ile Gln Leu
                145             150             155

aag agc aag ggg tct ttt ggc gat ttg gca gcc tgc act tat act ggt         531
Lys Ser Lys Gly Ser Phe Gly Asp Leu Ala Ala Cys Thr Tyr Thr Gly
                160             165             170

gtg atc cgc tac cag tcc ctg gat aga gaa tgg tta caa gaa caa atc         579
Val Ile Arg Tyr Gln Ser Leu Asp Arg Glu Trp Leu Gln Glu Gln Ile
        175             180             185

tcc aac cat tcc atc aag gac ctc ctg gcc atg gat tgg cct agc cta         627
Ser Asn His Ser Ile Lys Asp Leu Leu Ala Met Asp Trp Pro Ser Leu
        190             195             200

ggt cta gac cgg ctc agc ctg ccc cat gac ctc agg ctt tta atc gga         675
Gly Leu Asp Arg Leu Ser Leu Pro His Asp Leu Arg Leu Leu Ile Gly
205             210             215             220

tgg acc ggc cag cct gcc tcc aca gaa aaa ttg gtt cag gct gtc tac         723
Trp Thr Gly Gln Pro Ala Ser Thr Glu Lys Leu Val Gln Ala Val Tyr
```

```
                225                 230                 235

ccc caa aaa ata acc agg acc ccc ttg gac ttc cag tcc ttc tta gac     771
Pro Gln Lys Ile Thr Arg Thr Pro Leu Asp Phe Gln Ser Phe Leu Asp
            240                 245                 250

caa tcc caa gag tgt gtc gac ggc ttg gtg gag tct tta agc cag gct     819
Gln Ser Gln Glu Cys Val Asp Gly Leu Val Glu Ser Leu Ser Gln Ala
            255                 260                 265

gac tcc cag gca agc tta gct tgg atc caa aag aac cga acc ctc ctc     867
Asp Ser Gln Ala Ser Leu Ala Trp Ile Gln Lys Asn Arg Thr Leu Leu
            270                 275                 280

aag gca atg ggc caa agc cgg ggg aaa gtc atc gaa acc aaa gcc ttg     915
Lys Ala Met Gly Gln Ser Arg Gly Lys Val Ile Glu Thr Lys Ala Leu
        285                 290                 295                 300

acc tac ttg tgc gat att gtc gcg aaa tac gga ggc caa gcc aag tct     963
Thr Tyr Leu Cys Asp Ile Val Ala Lys Tyr Gly Gly Gln Ala Lys Ser
                305                 310                 315

tcc ggt gcc ggc ggt gga gat tgt ggc att ggc cta atc aca agg gag    1011
Ser Gly Ala Gly Gly Gly Asp Cys Gly Ile Gly Leu Ile Thr Arg Glu
                320                 325                 330

agc cca ata gaa gcc atc tac cgg gaa tgg atg gat gca ggt atc ttg    1059
Ser Pro Ile Glu Ala Ile Tyr Arg Glu Trp Met Asp Ala Gly Ile Leu
            335                 340                 345

ccc tta aga cta gac att gta gaa aat ggt gct tgc tat gac taa       1104
Pro Leu Arg Leu Asp Ile Val Glu Asn Gly Ala Cys Tyr Asp
        350                 355                 360


<210> 42
<211> 362
<212> PRT
<213> Alloiococcus otitidis

<400> 42
Met Val Tyr Ser Leu Arg Ile Pro Gly Lys Leu Tyr Leu Ala Gly Glu
1               5                   10                  15


Tyr Ala Val Val Thr Pro Gly Tyr Ala Gly Ile Leu Leu Thr Val Ser
                20                  25                  30


Arg Tyr Leu Thr Leu Asp Ile Trp Glu Thr Ser Pro Asp Gln Ala Ser
        35                  40                  45


Val Arg Ser Gln Thr Tyr Gly Asn Gln Ala Tyr Ala Trp Glu Arg Leu
    50                  55                  60
```

Asp Gly Ile Phe Ser Phe Lys Asp Trp Ser His Pro Phe His Leu Val
65   70   75   80

Glu Thr Val Ile Gln Thr Val Glu Ala Tyr Ile Glu Ser Leu Ser Leu
                85   90   .   95

Pro Leu Lys Ser Tyr Gly Ile Gln Ile Lys Ser Gln Leu Asp Tyr Gln
            100   105   110

Gly Lys Lys Ile Gly Leu Gly Ser Ser Gly Ala Val Thr Ile Ala Val
            115   120   125

Ile Arg Gly Leu Ser Leu Leu Tyr Asp Leu His Leu Lys Asp Ile Asp
    130   .   135   140

Ile Phe Lys Leu Ala Ala Ile Ala His Ile Gln Leu Lys Ser Lys Gly
145   150   155   160

Ser Phe Gly Asp Leu Ala Ala Cys Thr Tyr Thr Gly Val Ile Arg Tyr
            165   170   175

Gln Ser Leu Asp Arg Glu Trp Leu Gln Glu Gln Ile Ser Asn His Ser
            180   185   190

Ile Lys Asp Leu Leu Ala Met Asp Trp Pro Ser Leu Gly Leu Asp Arg
            195   200   205

Leu Ser Leu Pro His Asp Leu Arg Leu Leu Ile Gly Trp Thr Gly Gln
    210   215   220   .

Pro Ala Ser Thr Glu Lys Leu Val Gln Ala Val Tyr Pro Gln Lys Ile
225   230   235   240

Thr Arg Thr Pro Leu Asp Phe Gln Ser Phe Leu Asp Gln Ser Gln Glu
            245   250   255

Cys Val Asp Gly Leu Val Glu Ser Leu Ser Gln Ala Asp Ser Gln Ala
            260   265   270

Ser Leu Ala Trp Ile Gln Lys Asn Arg Thr Leu Leu Lys Ala Met Gly
    275   280   285

Gln Ser Arg Gly Lys Val Ile Glu Thr Lys Ala Leu Thr Tyr Leu Cys

```
              290                  295                  300

Asp Ile Val Ala Lys Tyr Gly Gly Gln Ala Lys Ser Ser Gly Ala Gly
305                 310                 315                 320


Gly Gly Asp Cys Gly Ile Gly Leu Ile Thr Arg Glu Ser Pro Ile Glu
                325                 330                 335


Ala Ile Tyr Arg Glu Trp Met Asp Ala Gly Ile Leu Pro Leu Arg Leu
                340                 345                 350


Asp Ile Val Glu Asn Gly Ala Cys Tyr Asp
                355                 360
```

<210> 43
<211> 1023
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (13)..(1023)
<223>

<400> 43

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gagaagccaa cc atg act aag cag gcc ttt gaa aag aaa aag tta ggc cgg     51
              Met Thr Lys Gln Ala Phe Glu Lys Lys Lys Leu Gly Arg
                1           5                  10


att tgc cgg gcc cat acc aac att gcc ttg atc aag tac tgg ggt aag     99
Ile Cys Arg Ala His Thr Asn Ile Ala Leu Ile Lys Tyr Trp Gly Lys
 15                  20                  25


gct gat agg gac ttg att atc ccc aat aac aac tcc cta tct tta acc    147
Ala Asp Arg Asp Leu Ile Ile Pro Asn Asn Asn Ser Leu Ser Leu Thr
 30                  35                  40                  45


ttg gac gct ttt tat acc gat acc cag gta gtt ttt gac cca gac ttg    195
Leu Asp Ala Phe Tyr Thr Asp Thr Gln Val Val Phe Asp Pro Asp Leu
                50                  55                  60


gac cag gac caa tta tgg cta gac ggg aaa cag gaa aaa ggg tcc gcc    243
Asp Gln Asp Gln Leu Trp Leu Asp Gly Lys Gln Glu Lys Gly Ser Ala
                65                  70                  75


tta acc aag gcc cag gtc atc ctg gac ttg gtt cgg gac caa gcc cag    291
Leu Thr Lys Ala Gln Val Ile Leu Asp Leu Val Arg Asp Gln Ala Gln
                80                  85                  90


ctt gac tgg ccg gcc aaa att acc agc cac aac caa gtt gcc act gca    339
Leu Asp Trp Pro Ala Lys Ile Thr Ser His Asn Gln Val Ala Thr Ala
                95                  100                 105
```

```
gct ggc ttg gct tcc tct gct tct ggt ctg gcc gcc ttg gcg ggt gct      387
Ala Gly Leu Ala Ser Ser Ala Ser Gly Leu Ala Ala Leu Ala Gly Ala
110             115             120             125

tca gct gat gct tta gac ctt ggc cta tcc cca act gac ctc tcc cga      435
Ser Ala Asp Ala Leu Asp Leu Gly Leu Ser Pro Thr Asp Leu Ser Arg
            130             135             140

ttg gcc cgc agg gga tct ggg tct gcc tca cga agt att ttt ggt ggt      483
Leu Ala Arg Arg Gly Ser Gly Ser Ala Ser Arg Ser Ile Phe Gly Gly
            145             150             155

ttt gtc gag tgg gaa aag ggt cat gat gat agc tct tcc ttt gcc aag      531
Phe Val Glu Trp Glu Lys Gly His Asp Asp Ser Ser Ser Phe Ala Lys
            160             165             170

ccc atc gac ttg gcc cag tgg gat att gcc atg ctc ttt gtc att gta      579
Pro Ile Asp Leu Ala Gln Trp Asp Ile Ala Met Leu Phe Val Ile Val
        175             180             185

agc gac cga cca aag gca att tcc tcc agc caa ggc atg caa ttg acc      627
Ser Asp Arg Pro Lys Ala Ile Ser Ser Ser Gln Gly Met Gln Leu Thr
190             195             200             205

cag gag acg tcg gac ttt tac cag gcc tgg tta gac agc ctg gac caa      675
Gln Glu Thr Ser Asp Phe Tyr Gln Ala Trp Leu Asp Ser Leu Asp Gln
            210             215             220

gac cta gca gac atc aag tcc gct atc caa gcc caa gac ctc gac cag      723
Asp Leu Ala Asp Ile Lys Ser Ala Ile Gln Ala Gln Asp Leu Asp Gln
            225             230             235

gtt ggg tcc att gca gaa aga aat gcc ctg aaa atg cat gcc acc aac      771
Val Gly Ser Ile Ala Glu Arg Asn Ala Leu Lys Met His Ala Thr Asn
            240             245             250

ctg gca gcc aag ccc ccc ttc acc tat tgg act aaa gaa agt tta gcc      819
Leu Ala Ala Lys Pro Pro Phe Thr Tyr Trp Thr Lys Glu Ser Leu Ala
            255             260             265

ctg atg cag gaa gta tgg gac cgg cgc aag gct ggc cag tcc ctc tac      867
Leu Met Gln Glu Val Trp Asp Arg Arg Lys Ala Gly Gln Ser Leu Tyr
270             275             280             285

ttc acc atg gac gcc ggc ccc aat gtc aag gtt att ggc agg gaa gct      915
Phe Thr Met Asp Ala Gly Pro Asn Val Lys Val Ile Gly Arg Glu Ala
            290             295             300

gac ctt aaa gcc ttc aaa gca gac ctc agc caa gac tgg ccc gac aag      963
Asp Leu Lys Ala Phe Lys Ala Asp Leu Ser Gln Asp Trp Pro Asp Lys
            305             310             315

cat ctt gtc tta gct aaa ccg ggt cca ggc ctg gcc ttt att gat gga     1011
His Leu Val Leu Ala Lys Pro Gly Pro Gly Leu Ala Phe Ile Asp Gly
            320             325             330
```

cct ttg aac tag   1023
Pro Leu Asn
    335

<210> 44
<211> 336
<212> PRT
<213> Alloiococcus otitidis

<400> 44
Met Thr Lys Gln Ala Phe Glu Lys Lys Lys Leu Gly Arg Ile Cys Arg
1   5   10   15

Ala His Thr Asn Ile Ala Leu Ile Lys Tyr Trp Gly Lys Ala Asp Arg
                20   25   30

Asp Leu Ile Ile Pro Asn Asn Asn Ser Leu Ser Leu Thr Leu Asp Ala
            35   40   45

Phe Tyr Thr Asp Thr Gln Val Val Phe Asp Pro Asp Leu Asp Gln Asp
    50   55   60

Gln Leu Trp Leu Asp Gly Lys Gln Glu Lys Gly Ser Ala Leu Thr Lys
65   70   75   80

Ala Gln Val Ile Leu Asp Leu Val Arg Asp Gln Ala Gln Leu Asp Trp
                85   90   95

Pro Ala Lys Ile Thr Ser His Asn Gln Val Ala Thr Ala Ala Gly Leu
                100   105   110

Ala Ser Ser Ala Ser Gly Leu Ala Ala Leu Ala Gly Ala Ser Ala Asp
            115   120   125

Ala Leu Asp Leu Gly Leu Ser Pro Thr Asp Leu Ser Arg Leu Ala Arg
        130   135   140

Arg Gly Ser Gly Ser Ala Ser Arg Ser Ile Phe Gly Gly Phe Val Glu
145   150   155   160

Trp Glu Lys Gly His Asp Asp Ser Ser Ser Phe Ala Lys Pro Ile Asp
                165   170   175

Leu Ala Gln Trp Asp Ile Ala Met Leu Phe Val Ile Val Ser Asp Arg
            180   185   190

```
Pro Lys Ala Ile Ser Ser Ser Gln Gly Met Gln Leu Thr Gln Glu Thr
        195             200             205


Ser Asp Phe Tyr Gln Ala Trp Leu Asp Ser Leu Asp Gln Asp Leu Ala
        210             215             220


Asp Ile Lys Ser Ala Ile Gln Ala Gln Asp Leu Asp Gln Val Gly Ser
225             230             235             240


Ile Ala Glu Arg Asn Ala Leu Lys Met His Ala Thr Asn Leu Ala Ala
            245             250             255


Lys Pro Pro Phe Thr Tyr Trp Thr Lys Glu Ser Leu Ala Leu Met Gln
            260             265             270


Glu Val Trp Asp Arg Arg Lys Ala Gly Gln Ser Leu Tyr Phe Thr Met
        275             280             285


Asp Ala Gly Pro Asn Val Lys Val Ile Gly Arg Glu Ala Asp Leu Lys
        290             295             300


Ala Phe Lys Ala Asp Leu Ser Gln Asp Trp Pro Asp Lys His Leu Val
305             310             315             320


Leu Ala Lys Pro Gly Pro Gly Leu Ala Phe Ile Asp Gly Pro Leu Asn
            325             330             335
```

```
<210> 45
<211> 981
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (28)..(981)
<223>

<400> 45
acaaaaatag acaaaggaga caaaagg atg acg ctt gtt aaa aat gta gcc aaa      54
                               Met Thr Leu Val Lys Asn Val Ala Lys
                                1               5

ggc act gcc cat ggt aaa att att tta atc ggt gag cat gct gtt gtc     102
```

```
                Gly Thr Ala His Gly Lys Ile Ile Leu Ile Gly Glu His Ala Val Val
                10              15                  20              25

tat aac atg ccg gcc atc gcc ctc cct ttt acc aca gcc acc atc acc        150
Tyr Asn Met Pro Ala Ile Ala Leu Pro Phe Thr Thr Ala Thr Ile Thr
                        30              35              40

gtt gaa gtt agt cct tac caa ggc aaa agc tat cta gaa agt gct tgc        198
Val Glu Val Ser Pro Tyr Gln Gly Lys Ser Tyr Leu Glu Ser Ala Cys
                    45              50              55

tac tgc gga tct tta gac caa gcg ccc ggg gac ttg gca ggg ctt caa        246
Tyr Cys Gly Ser Leu Asp Gln Ala Pro Gly Asp Leu Ala Gly Leu Gln
                60              65              70

gcc tgt ttg aca gcg gtt tgt gcc gac tta gac cag tcc agc gac cac        294
Ala Cys Leu Thr Ala Val Cys Ala Asp Leu Asp Gln Ser Ser Asp His
            75              80              85

ttg tat atc aag gtc gac agc atg atc cct gct gaa aga gga atg ggg        342
Leu Tyr Ile Lys Val Asp Ser Met Ile Pro Ala Glu Arg Gly Met Gly
90              95              100             105

tcc agt gct gct gtg gcc acc gcc tta gtc aag gcc ctc ttt cac tac        390
Ser Ser Ala Ala Val Ala Thr Ala Leu Val Lys Ala Leu Phe His Tyr
                110             115             120

ttc caa gtc gac tta agc agt gaa gcc ctc tca gcc tat gtc gag att        438
Phe Gln Val Asp Leu Ser Ser Glu Ala Leu Ser Ala Tyr Val Glu Ile
                125             130             135

gcc gaa aaa att acc cat ggc aag cca tcg ggt ctg gat gct aca gtc        486
Ala Glu Lys Ile Thr His Gly Lys Pro Ser Gly Leu Asp Ala Thr Val
            140             145             150

gtc aac tcc att gcc ccc gtt tat ttt aaa cgc aac cag ctt ccc aag        534
Val Asn Ser Ile Ala Pro Val Tyr Phe Lys Arg Asn Gln Leu Pro Lys
        155             160             165

gcc atc cct tta aat gtt gac ggc tat tta att gca gcc gat act ggg        582
Ala Ile Pro Leu Asn Val Asp Gly Tyr Leu Ile Ala Ala Asp Thr Gly
170             175             180             185

att aag ggc cac acg aaa gaa gcc gtt ggg gat gtg gcg aag ctg gtt        630
Ile Lys Gly His Thr Lys Glu Ala Val Gly Asp Val Ala Lys Leu Val
                190             195             200

gaa act gcc aag gtt caa acc atg gac att gtc cac cac ctc ggc cag        678
Glu Thr Ala Lys Val Gln Thr Met Asp Ile Val His His Leu Gly Gln
            205             210             215

ctt acc cac cag gct aaa aaa gca atc atg acc aat aac ctc cct ggc        726
Leu Thr His Gln Ala Lys Lys Ala Ile Met Thr Asn Asn Leu Pro Gly
            220             225             230

tta ggg gag att ttg aac cag tcc cac caa ctc tta aag gat tta act        774
Leu Gly Glu Ile Leu Asn Gln Ser His Gln Leu Leu Lys Asp Leu Thr
```

```
            235                 240                 245
gtc agc aat ccc aag tta gac caa ctt gtc caa gca gcc caa gat gct    822
Val Ser Asn Pro Lys Leu Asp Gln Leu Val Gln Ala Ala Gln Asp Ala
250                 255                 260                 265

gga gct tgc gga gct aag tta acc ggt ggg ggc cgg ggt ggt tgc atg    870
Gly Ala Cys Gly Ala Lys Leu Thr Gly Gly Gly Arg Gly Gly Cys Met
                    270                 275                 280

att gcc cta gcc caa agc aac cag gat gcc tcc aat att gcc caa aaa    918
Ile Ala Leu Ala Gln Ser Asn Gln Asp Ala Ser Asn Ile Ala Gln Lys
                285                 290                 295

ttg gaa aaa gcg gga gcc att gaa acc tgg atc cac ccc tta gga gaa    966
Leu Glu Lys Ala Gly Ala Ile Glu Thr Trp Ile His Pro Leu Gly Glu
            300                 305                 310

gcc aac cat gac taa                                                981
Ala Asn His Asp
        315


<210> 46
<211> 317
<212> PRT
<213> Alloiococcus otitidis

<400> 46
Met Thr Leu Val Lys Asn Val Ala Lys Gly Thr Ala His Gly Lys Ile
1               5                   10                  15


Ile Leu Ile Gly Glu His Ala Val Val Tyr Asn Met Pro Ala Ile Ala
            20                  25                  30


Leu Pro Phe Thr Thr Ala Thr Ile Thr Val Glu Val Ser Pro Tyr Gln
        35                  40                  45


Gly Lys Ser Tyr Leu Glu Ser Ala Cys Tyr Cys Gly Ser Leu Asp Gln
    50                  55                  60


Ala Pro Gly Asp Leu Ala Gly Leu Gln Ala Cys Leu Thr Ala Val Cys
65                  70                  75                  80


Ala Asp Leu Asp Gln Ser Ser Asp His Leu Tyr Ile Lys Val Asp Ser
                85                  90                  95


Met Ile Pro Ala Glu Arg Gly Met Gly Ser Ser Ala Ala Val Ala Thr
            100                 105                 110
```

```
Ala Leu Val Lys Ala Leu Phe His Tyr Phe Gln Val Asp Leu Ser Ser
        115             120             125

Glu Ala Leu Ser Ala Tyr Val Glu Ile Ala Glu Lys Ile Thr His Gly
    130             135             140

Lys Pro Ser Gly Leu Asp Ala Thr Val Val Asn Ser Ile Ala Pro Val
145             150             155             160

Tyr Phe Lys Arg Asn Gln Leu Pro Lys Ala Ile Pro Leu Asn Val Asp
            165             170             175

Gly Tyr Leu Ile Ala Ala Asp Thr Gly Ile Lys Gly His Thr Lys Glu
            180             185             190

Ala Val Gly Asp Val Ala Lys Leu Val Glu Thr Ala Lys Val Gln Thr
        195             200             205

Met Asp Ile Val His His Leu Gly Gln Leu Thr His Gln Ala Lys Lys
    210             215             220

Ala Ile Met Thr Asn Asn Leu Pro Gly Leu Gly Glu Ile Leu Asn Gln
225             230             235             240

Ser His Gln Leu Leu Lys Asp Leu Thr Val Ser Asn Pro Lys Leu Asp
            245             250             255

Gln Leu Val Gln Ala Ala Gln Asp Ala Gly Ala Cys Gly Ala Lys Leu
        260             265             270

Thr Gly Gly Gly Arg Gly Gly Cys Met Ile Ala Leu Ala Gln Ser Asn
        275             280             285

Gln Asp Ala Ser Asn Ile Ala Gln Lys Leu Glu Lys Ala Gly Ala Ile
    290             295             300

Glu Thr Trp Ile His Pro Leu Gly Glu Ala Asn His Asp
305             310             315
```

<210> 47
<211> 975
<212> DNA
<213> Alloiococcus otitidis

```
<220>
<221> CDS
<222> (46)..(975)
<223>

<400> 47
agaatcaaat ttgttttaaa attatcagct tttggaggtc agaac atg aac aat tcc        57
                                                     Met Asn Asn Ser
                                                      1

cgt att ttt tta gtc tat gac cgt aaa gac tgg cag tct ctt aga gaa         105
Arg Ile Phe Leu Val Tyr Asp Arg Lys Asp Trp Gln Ser Leu Arg Glu
 5               10                  15                  20

aat gcc agc ctt tct tta acg gaa aaa aac cta aat aac ttg cgt gca         153
Asn Ala Ser Leu Ser Leu Thr Glu Lys Asn Leu Asn Asn Leu Arg Ala
                25                  30                  35

gtg aat gac gtc ata tcg atg gaa gat gtc cga gaa gtt tac gtc ccc         201
Val Asn Asp Val Ile Ser Met Glu Asp Val Arg Glu Val Tyr Val Pro
                40                  45                  50

att atc caa tta ctg gat gtc tac ata aaa agt tac tac cgc cac cag         249
Ile Ile Gln Leu Leu Asp Val Tyr Ile Lys Ser Tyr Tyr Arg His Gln
            55                  60                  65

gct tcc ttg atc aat tac ttg aac ctg gac cag cct aaa aag tac caa         297
Ala Ser Leu Ile Asn Tyr Leu Asn Leu Asp Gln Pro Lys Lys Tyr Gln
        70                  75                  80

ccc tat gtg att ggg att gca ggg agc gtg gct gtg ggc aag tct acg         345
Pro Tyr Val Ile Gly Ile Ala Gly Ser Val Ala Val Gly Lys Ser Thr
85                  90                  95                  100

gtt gcc agg ctt ctt aag tcc ctc ttg agc gac tac tat ccg gaa aaa         393
Val Ala Arg Leu Leu Lys Ser Leu Leu Ser Asp Tyr Tyr Pro Glu Lys
                105                 110                 115

aag gta gac ctc ctc aca aca gat ggc ttc ctt tat ccg aat aag att         441
Lys Val Asp Leu Leu Thr Thr Asp Gly Phe Leu Tyr Pro Asn Lys Ile
                120                 125                 130

tta aaa gag cga gat atc atg gac cgc aag ggt ttt ccc gaa agc tat         489
Leu Lys Glu Arg Asp Ile Met Asp Arg Lys Gly Phe Pro Glu Ser Tyr
                135                 140                 145

gat atg aaa cgt ttg att aac ttt atg acc gat gtc aaa aat aat gtt         537
Asp Met Lys Arg Leu Ile Asn Phe Met Thr Asp Val Lys Asn Asn Val
    150                 155                 160

ccc aac atc cag gtg ccc aag tat tcc cac caa gtt tac gac ata gta         585
Pro Asn Ile Gln Val Pro Lys Tyr Ser His Gln Val Tyr Asp Ile Val
165                 170                 175                 180

gaa ggg gaa agg ttg acc att aac cag cca gac atc ttg att gtc gaa         633
Glu Gly Glu Arg Leu Thr Ile Asn Gln Pro Asp Ile Leu Ile Val Glu
                185                 190                 195
```

```
ggg atc aat gtg ctc caa ctt cct tct aat gag aag att ttt gtt agc     681
Gly Ile Asn Val Leu Gln Leu Pro Ser Asn Glu Lys Ile Phe Val Ser
            200             205             210

gat ttt ttc gac ttc tcc ttt tat gtg gat gcc tca gaa aat ctg att     729
Asp Phe Phe Asp Phe Ser Phe Tyr Val Asp Ala Ser Glu Asn Leu Ile
            215             220             225

gaa aaa tgg tac atg caa cgc ttt ggc acc ttt atg gat acc gcc ttc     777
Glu Lys Trp Tyr Met Gln Arg Phe Gly Thr Phe Met Asp Thr Ala Phe
            230             235             240

caa gac ccc aac aac tat tac tac aag ttt aat gac tgg gac cgc aag     825
Gln Asp Pro Asn Asn Tyr Tyr Tyr Lys Phe Asn Asp Trp Asp Arg Lys
245             250             255             260

gaa gct ttt gcc tat gcc aac caa gtt tgg gaa acg gtt aac cta gaa     873
Glu Ala Phe Ala Tyr Ala Asn Gln Val Trp Glu Thr Val Asn Leu Glu
            265             270             275

aac ctc agg gaa tat att cta ccc acc cga ctc cgg gct aac ctc atc     921
Asn Leu Arg Glu Tyr Ile Leu Pro Thr Arg Leu Arg Ala Asn Leu Ile
            280             285             290

ctc cat aaa acc cat aac cac tac atc gac aag att tta ctc aaa aaa     969
Leu His Lys Thr His Asn His Tyr Ile Asp Lys Ile Leu Leu Lys Lys
            295             300             305

cac tga                                                             975
His
```

<210> 48
<211> 309
<212> PRT
<213> Alloiococcus otitidis

<400> 48
```
Met Asn Asn Ser Arg Ile Phe Leu Val Tyr Asp Arg Lys Asp Trp Gln
1               5               10              15

Ser Leu Arg Glu Asn Ala Ser Leu Ser Leu Thr Glu Lys Asn Leu Asn
            20              25              30

Asn Leu Arg Ala Val Asn Asp Val Ile Ser Met Glu Asp Val Arg Glu
            35              40              45

Val Tyr Val Pro Ile Ile Gln Leu Leu Asp Val Tyr Ile Lys Ser Tyr
    50              55              60

Tyr Arg His Gln Ala Ser Leu Ile Asn Tyr Leu Asn Leu Asp Gln Pro
65              70              75              80
```

```
Lys Lys Tyr Gln Pro Tyr Val Ile Gly Ile Ala Gly Ser Val Ala Val
            85              90              95

Gly Lys Ser Thr Val Ala Arg Leu Leu Lys Ser Leu Leu Ser Asp Tyr
            100             105             110

Tyr Pro Glu Lys Lys Val Asp Leu Leu Thr Thr Asp Gly Phe Leu Tyr
        115             120             125

Pro Asn Lys Ile Leu Lys Glu Arg Asp Ile Met Asp Arg Lys Gly Phe
        130             135             140

Pro Glu Ser Tyr Asp Met Lys Arg Leu Ile Asn Phe Met Thr Asp Val
145             150             155             160

Lys Asn Asn Val Pro Asn Ile Gln Val Pro Lys Tyr Ser His Gln Val
                165             170             175

Tyr Asp Ile Val Glu Gly Glu Arg Leu Thr Ile Asn Gln Pro Asp Ile
            180             185             190

Leu Ile Val Glu Gly Ile Asn Val Leu Gln Leu Pro Ser Asn Glu Lys
        195             200             205

Ile Phe Val Ser Asp Phe Phe Asp Phe Ser Phe Tyr Val Asp Ala Ser
    210             215             220

Glu Asn Leu Ile Glu Lys Trp Tyr Met Gln Arg Phe Gly Thr Phe Met
225             230             235             240

Asp Thr Ala Phe Gln Asp Pro Asn Asn Tyr Tyr Tyr Lys Phe Asn Asp
            245             250             255

Trp Asp Arg Lys Glu Ala Phe Ala Tyr Ala Asn Gln Val Trp Glu Thr
        260             265             270

Val Asn Leu Glu Asn Leu Arg Glu Tyr Ile Leu Pro Thr Arg Leu Arg
        275             280             285

Ala Asn Leu Ile Leu His Lys Thr His Asn His Tyr Ile Asp Lys Ile
    290             295             300
```

Leu Leu Lys Lys His
305

<210> 49
<211> 846
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (7)..(846)
<223>

<400> 49
agctta atg gga gac gat tta aga gaa gaa att ctt gac cga atg aag   48
       Met Gly Asp Asp Leu Arg Glu Glu Ile Leu Asp Arg Met Lys
        1   5   10

gtc caa gcc caa att aac ccc aat gag gaa att cgc cgg acc att gac   96
Val Gln Ala Gln Ile Asn Pro Asn Glu Glu Ile Arg Arg Thr Ile Asp
15   20   25   30

ttt atc aag gac tat ctc cag gcc cac ccc ttc ttt gaa tcc tta atc   144
Phe Ile Lys Asp Tyr Leu Gln Ala His Pro Phe Phe Glu Ser Leu Ile
                35   40   45

ttg ggc atc tcc ggt ggc cag gat tcc acc ctc ctg ggt aag cta gcc   192
Leu Gly Ile Ser Gly Gly Gln Asp Ser Thr Leu Leu Gly Lys Leu Ala
                50   55   60

cag atg gcc tgc ctt gaa ctg agg gaa gag gag ggg tct gac aag cca   240
Gln Met Ala Cys Leu Glu Leu Arg Glu Glu Glu Gly Ser Asp Lys Pro
            65   70   75

att ttt att ggt atc cgc cta cct tat ggg gat caa ttt gat gaa gca   288
Ile Phe Ile Gly Ile Arg Leu Pro Tyr Gly Asp Gln Phe Asp Glu Ala
            80   85   90

gaa gcc cag caa gcc ctc aat tgg atc cag cct gac cag gct ctg acc   336
Glu Ala Gln Gln Ala Leu Asn Trp Ile Gln Pro Asp Gln Ala Leu Thr
95   100   105   110

att aat atc aaa gag tcc gtt gat ggc ctg gtt gac act ttg gcc ggc   384
Ile Asn Ile Lys Glu Ser Val Asp Gly Leu Val Asp Thr Leu Ala Gly
                115   120   125

caa ggc att gaa gtt tct gac ttt aac aag ggc aat atc aaa gct cgg   432
Gln Gly Ile Glu Val Ser Asp Phe Asn Lys Gly Asn Ile Lys Ala Arg
                130   135   140

atc cga atg gtg gcc caa tat ggc gta gcg ggt cac ttc cac ggg gcg   480
Ile Arg Met Val Ala Gln Tyr Gly Val Ala Gly His Phe His Gly Ala
            145   150   155

gtg tta gga tct gac cat tca gcc gaa aat gta act ggc ttt ttc acc   528

```
Val Leu Gly Ser Asp His Ser Ala Glu Asn Val Thr Gly Phe Phe Thr
    160             165             170

aag cat ggg gac ggc gct agt gac ctc aac cct ctt ttc cgc cta aat      576
Lys His Gly Asp Gly Ala Ser Asp Leu Asn Pro Leu Phe Arg Leu Asn
175             180             185             190

aaa cgt cag gga cgg gcc ctg ctt gag gaa tta ggg tcc cct aag aac      624
Lys Arg Gln Gly Arg Ala Leu Leu Glu Glu Leu Gly Ser Pro Lys Asn
                195             200             205

ttg tac caa aag acc ccc aca gct gat ttg gaa gaa gac cag ccc ggc      672
Leu Tyr Gln Lys Thr Pro Thr Ala Asp Leu Glu Glu Asp Gln Pro Gly
                210             215             220

ttg tca gat gaa gac aag tta ggg gtt tct tat gaa gcc att gat gac      720
Leu Ser Asp Glu Asp Lys Leu Gly Val Ser Tyr Glu Ala Ile Asp Asp
        225             230             235

tac ttg gag ggc aag cca gtt agc cag gag gac cag gca acc atc gaa      768
Tyr Leu Glu Gly Lys Pro Val Ser Gln Glu Asp Gln Ala Thr Ile Glu
    240             245             250

aaa tgg tat caa caa acg gcc cac aag cgc cac ttg ccg gtg act atc      816
Lys Trp Tyr Gln Gln Thr Ala His Lys Arg His Leu Pro Val Thr Ile
255             260             265             270

ttt gat gat ttt tgg aaa gaa aaa aat tag                             846
Phe Asp Asp Phe Trp Lys Glu Lys Asn
                275
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<210> 50
<211> 279
<212> PRT
<213> Alloiococcus otitidis

<400> 50
Met Gly Asp Asp Leu Arg Glu Glu Ile Leu Asp Arg Met Lys Val Gln
1               5               10              15


Ala Gln Ile Asn Pro Asn Glu Glu Ile Arg Arg Thr Ile Asp Phe Ile
            20              25              30


Lys Asp Tyr Leu Gln Ala His Pro Phe Phe Glu Ser Leu Ile Leu Gly
        35              40              45


Ile Ser Gly Gly Gln Asp Ser Thr Leu Leu Gly Lys Leu Ala Gln Met
    50              55              60


Ala Cys Leu Glu Leu Arg Glu Glu Glu Gly Ser Asp Lys Pro Ile Phe
65              70              75              80
```

Ile Gly Ile Arg Leu Pro Tyr Gly Asp Gln Phe Asp Glu Ala Glu Ala
              85   90   95

Gln Gln Ala Leu Asn Trp Ile Gln Pro Asp Gln Ala Leu Thr Ile Asn
              100   105   110

Ile Lys Glu Ser Val Asp Gly Leu Val Asp Thr Leu Ala Gly Gln Gly
              115   120   125

Ile Glu Val Ser Asp Phe Asn Lys Gly Asn Ile Lys Ala Arg Ile Arg
          130   135   140

Met Val Ala Gln Tyr Gly Val Ala Gly His Phe His Gly Ala Val Leu
145   150   155   160

Gly Ser Asp His Ser Ala Glu Asn Val Thr Gly Phe Phe Thr Lys His
              165   170   175

Gly Asp Gly Ala Ser Asp Leu Asn Pro Leu Phe Arg Leu Asn Lys Arg
              180   185   190

Gln Gly Arg Ala Leu Leu Glu Glu Leu Gly Ser Pro Lys Asn Leu Tyr
              195   200   205

Gln Lys Thr Pro Thr Ala Asp Leu Glu Glu Asp Gln Pro Gly Leu Ser
          210   215   220

Asp Glu Asp Lys Leu Gly Val Ser Tyr Glu Ala Ile Asp Asp Tyr Leu
225   230   235   240

Glu Gly Lys Pro Val Ser Gln Glu Asp Gln Ala Thr Ile Glu Lys Trp
              245   250   255

Tyr Gln Gln Thr Ala His Lys Arg His Leu Pro Val Thr Ile Phe Asp
              260   265   270

Asp Phe Trp Lys Glu Lys Asn
          275

<210> 51
<211> 843
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (7)..(843)
<223>

<400> 51

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aggaac atg att atg tat act gat ggg att ggc ttt att gat tca gga        48
       Met Ile Met Tyr Thr Asp Gly Ile Gly Phe Ile Asp Ser Gly
       1           5                   10

gtg ggt ggc ttc acc ctg gtc aaa gaa gcc atg aag caa ttg cca aat      96
Val Gly Gly Phe Thr Leu Val Lys Glu Ala Met Lys Gln Leu Pro Asn
15              20                  25                  30

gaa caa ttt tac tat ctg gga gac acc gcc cgg tca cct tat gga cct     144
Glu Gln Phe Tyr Tyr Leu Gly Asp Thr Ala Arg Ser Pro Tyr Gly Pro
                35                  40                  45

aaa gac atg gcc act gtc aag gca tat gcc ttt gaa ctt gcc aat tac     192
Lys Asp Met Ala Thr Val Lys Ala Tyr Ala Phe Glu Leu Ala Asn Tyr
            50                  55                  60

ctg gtt aaa aac cac cag atc aaa atc ttg gtg atc gct tgt aat act     240
Leu Val Lys Asn His Gln Ile Lys Ile Leu Val Ile Ala Cys Asn Thr
            65                  70                  75

gcg act gtc gct gcc ctc aag gac cta aaa cag gcc ttg ccc atc cca     288
Ala Thr Val Ala Ala Leu Lys Asp Leu Lys Gln Ala Leu Pro Ile Pro
        80                  85                  90

gtt tta ggg gtc atc tta cct ggt tgc cga gca gct att aag gct agt     336
Val Leu Gly Val Ile Leu Pro Gly Cys Arg Ala Ala Ile Lys Ala Ser
95                  100                 105                 110

gtt aac cat cag att ggg gtt att gcc acc cat ggg acc atc cag tcc     384
Val Asn His Gln Ile Gly Val Ile Ala Thr His Gly Thr Ile Gln Ser
                115                 120                 125

ggt cgc tat gag ctt gaa ctt aaa cgg aaa cga ccg gat att gaa gtg     432
Gly Arg Tyr Glu Leu Glu Leu Lys Arg Lys Arg Pro Asp Ile Glu Val
            130                 135                 140

aca agt ctg gct tgt ccc gaa ttt gcc ccc atg gta gag gcg gga gac     480
Thr Ser Leu Ala Cys Pro Glu Phe Ala Pro Met Val Glu Ala Gly Asp
            145                 150                 155

tac cga tct gtt caa gct agc agt gtg gtg agg aca tcc tta cag gcc     528
Tyr Arg Ser Val Gln Ala Ser Ser Val Val Arg Thr Ser Leu Gln Ala
        160                 165                 170

cta gaa gac caa gat ttg gat acc ctt att ttg ggt tgc acc cac tat     576
Leu Glu Asp Gln Asp Leu Asp Thr Leu Ile Leu Gly Cys Thr His Tyr
175                 180                 185                 190

ccc att ata aaa gac ctc att caa gac tct att ggc cct ggt atc agc     624
Pro Ile Ile Lys Asp Leu Ile Gln Asp Ser Ile Gly Pro Gly Ile Ser
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                    195   200   205

ttg gtt gat cca ggg gcg gaa gct gtg aat gac ttg agt gtc tta tta   672
Leu Val Asp Pro Gly Ala Glu Ala Val Asn Asp Leu Ser Val Leu Leu
            210   215   220

gac tat tat gac ttg act aat gac cgg ttt aat ccc aac ctg acc cac   720
Asp Tyr Tyr Asp Leu Thr Asn Asp Arg Phe Asn Pro Asn Leu Thr His
            225   230   235

cat ttt tac acc acg gga gat aaa gcc ggg ttt aag aaa atc gcg gat   768
His Phe Tyr Thr Thr Gly Asp Lys Ala Gly Phe Lys Lys Ile Ala Asp
        240   245   250

gac tgg ctt gac cac cac aac tac cgg gtt gac cat tta gat tta gag   816
Asp Trp Leu Asp His His Asn Tyr Arg Val Asp His Leu Asp Leu Glu
255   260   265   270

gag ttg caa gaa gtt aat gga aga taa   843
Glu Leu Gln Glu Val Asn Gly Arg
                275

<210> 52
<211> 278
<212> PRT
<213> Alloiococcus otitidis

<400> 52
Met Ile Met Tyr Thr Asp Gly Ile Gly Phe Ile Asp Ser Gly Val Gly
1   5   10   15

Gly Phe Thr Leu Val Lys Glu Ala Met Lys Gln Leu Pro Asn Glu Gln
            20   25   30

Phe Tyr Tyr Leu Gly Asp Thr Ala Arg Ser Pro Tyr Gly Pro Lys Asp
        35   40   45

Met Ala Thr Val Lys Ala Tyr Ala Phe Glu Leu Ala Asn Tyr Leu Val
    50   55   60

Lys Asn His Gln Ile Lys Ile Leu Val Ile Ala Cys Asn Thr Ala Thr
65   70   75   80

Val Ala Ala Leu Lys Asp Leu Lys Gln Ala Leu Pro Ile Pro Val Leu
            85   90   95

Gly Val Ile Leu Pro Gly Cys Arg Ala Ala Ile Lys Ala Ser Val Asn
            100   105   110

His Gln Ile Gly Val Ile Ala Thr His Gly Thr Ile Gln Ser Gly Arg
        115   120   125

Tyr Glu Leu Glu Leu Lys Arg Lys Arg Pro Asp Ile Glu Val Thr Ser
    130   135   140

Leu Ala Cys Pro Glu Phe Ala Pro Met Val Glu Ala Gly Asp Tyr Arg
145   150   155   160

Ser Val Gln Ala Ser Ser Val Val Arg Thr Ser Leu Gln Ala Leu Glu
                165   170   175

Asp Gln Asp Leu Asp Thr Leu Ile Leu Gly Cys Thr His Tyr Pro Ile
                180   185   190

Ile Lys Asp Leu Ile Gln Asp Ser Ile Gly Pro Gly Ile Ser Leu Val
        195   200   205

Asp Pro Gly Ala Glu Ala Val Asn Asp Leu Ser Val Leu Leu Asp Tyr
    210   215   220

Tyr Asp Leu Thr Asn Asp Arg Phe Asn Pro Asn Leu Thr His His Phe
225   230   235   240

Tyr Thr Thr Gly Asp Lys Ala Gly Phe Lys Lys Ile Ala Asp Asp Trp
                245   250   255

Leu Asp His His Asn Tyr Arg Val Asp His Leu Asp Leu Glu Glu Leu
                260   265   270

Gln Glu Val Asn Gly Arg
        275

<210> 53
<211> 957
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (7)..(957)
<223>

<400> 53
aaaaat atg acg aag gag tct tca ttt atg gtc aag acc aaa ata tgt   48
       Met Thr Lys Glu Ser Ser Phe Met Val Lys Thr Lys Ile Cys

```
          1                5                  10
tct att tta aat ata aca ccg gat tca ttt tct gat ggt ggg cgc aac      96
Ser Ile Leu Asn Ile Thr Pro Asp Ser Phe Ser Asp Gly Gly Arg Asn
15                  20              25                  30

tat cag gca gac caa gcc ata gct cac gga ctc gac ttg gta gac aag     144
Tyr Gln Ala Asp Gln Ala Ile Ala His Gly Leu Asp Leu Val Asp Lys
                35              40                  45

gga gcg gac atg ttg gat att gga ggt gag tcg acc cgg cct ggt tcc     192
Gly Ala Asp Met Leu Asp Ile Gly Gly Glu Ser Thr Arg Pro Gly Ser
            50              55                  60

agt cca gtc gac ctc caa gat gaa atc gac cgt att gta ccg gtg atc     240
Ser Pro Val Asp Leu Gln Asp Glu Ile Asp Arg Ile Val Pro Val Ile
            65              70                  75

aag gga atc aga gaa aaa agt cag gtt cct att tca gta gat acc tac     288
Lys Gly Ile Arg Glu Lys Ser Gln Val Pro Ile Ser Val Asp Thr Tyr
            80              85                  90

cgg gct cca gtt gcc aaa gcg gct att gat gct ggg gcg gat atc atc     336
Arg Ala Pro Val Ala Lys Ala Ala Ile Asp Ala Gly Ala Asp Ile Ile
95                  100             105                 110

aat gat att acc ggt cta act ggt gat gta gac atg gcc gac ttg cta     384
Asn Asp Ile Thr Gly Leu Thr Gly Asp Val Asp Met Ala Asp Leu Leu
                115             120                 125

gct caa gaa ggg gtt aag gcc att gtc atg ttc aac ccg gtt att gct     432
Ala Gln Glu Gly Val Lys Ala Ile Val Met Phe Asn Pro Val Ile Ala
            130             135                 140

cga cct gac cac cca tct tcc caa aaa ttc aga gat ttc ggg ggc cga     480
Arg Pro Asp His Pro Ser Ser Gln Lys Phe Arg Asp Phe Gly Gly Arg
            145             150                 155

gat ttt ttc acc gat gaa gaa aga gat aaa atg tcc caa gca ccc att     528
Asp Phe Phe Thr Asp Glu Glu Arg Asp Lys Met Ser Gln Ala Pro Ile
            160             165                 170

gaa gag gcc atg atg gtc tac ttt gac aaa gtc ttg aac aag gcc cat     576
Glu Glu Ala Met Met Val Tyr Phe Asp Lys Val Leu Asn Lys Ala His
175                 180             185                 190

caa gct ggg att gac cgg gat aag att tta ctg gac ccg gga att ggc     624
Gln Ala Gly Ile Asp Arg Asp Lys Ile Leu Leu Asp Pro Gly Ile Gly
                195             200                 205

ttt ggc ctg acc aag aag gaa aat tac aag ttg att cac agt gtt gcc     672
Phe Gly Leu Thr Lys Lys Glu Asn Tyr Lys Leu Ile His Ser Val Ala
            210             215                 220

tcg att cat gac aag ggc tac ccg gtc ttt tta gga gtt tcc cgc aaa     720
Ser Ile His Asp Lys Gly Tyr Pro Val Phe Leu Gly Val Ser Arg Lys
            225             230                 235
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cgc ttc ttg gtg ggg gaa gtc tcc aag cta ggc atc gaa gcc gac cca        768
Arg Phe Leu Val Gly Glu Val Ser Lys Leu Gly Ile Glu Ala Asp Pro
    240             245             250

gag acc caa gca gga ttt tta aac cga gac ctg gct tca gct att att        816
Glu Thr Gln Ala Gly Phe Leu Asn Arg Asp Leu Ala Ser Ala Ile Ile
255             260             265             270

aca gct tac gct agc cat ata ggg gta gac tat gtc cgg gtt cat tcc        864
Thr Ala Tyr Ala Ser His Ile Gly Val Asp Tyr Val Arg Val His Ser
            275             280             285

tta gat gaa cac aaa ata gca acc acc att acc cat aat att tta aac        912
Leu Asp Glu His Lys Ile Ala Thr Thr Ile Thr His Asn Ile Leu Asn
            290             295             300

agc gat agc tta gat gat cag agc ttt gac caa tat aaa aat taa          957
Ser Asp Ser Leu Asp Asp Gln Ser Phe Asp Gln Tyr Lys Asn
            305             310             315
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<210> 54
<211> 316
<212> PRT
<213> Alloiococcus otitidis

<400> 54

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Met Thr Lys Glu Ser Ser Phe Met Val Lys Thr Lys Ile Cys Ser Ile
1               5               10              15


Leu Asn Ile Thr Pro Asp Ser Phe Ser Asp Gly Gly Arg Asn Tyr Gln
            20              25              30


Ala Asp Gln Ala Ile Ala His Gly Leu Asp Leu Val Asp Lys Gly Ala
        35              40              45


Asp Met Leu Asp Ile Gly Gly Glu Ser Thr Arg Pro Gly Ser Ser Pro
    50              55              60


Val Asp Leu Gln Asp Glu Ile Asp Arg Ile Val Pro Val Ile Lys Gly
65              70              75              80


Ile Arg Glu Lys Ser Gln Val Pro Ile Ser Val Asp Thr Tyr Arg Ala
            85              90              95


Pro Val Ala Lys Ala Ala Ile Asp Ala Gly Ala Asp Ile Ile Asn Asp
            100             105             110


Ile Thr Gly Leu Thr Gly Asp Val Asp Met Ala Asp Leu Leu Ala Gln
```

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                 115                   120                   125

    Glu Gly Val Lys Ala Ile Val Met Phe Asn Pro Val Ile Ala Arg Pro
        130                 135                 140

    Asp His Pro Ser Ser Gln Lys Phe Arg Asp Phe Gly Gly Arg Asp Phe
    145                 150                 155                 160

    Phe Thr Asp Glu Glu Arg Asp Lys Met Ser Gln Ala Pro Ile Glu Glu
                165                 170                 175

    Ala Met Met Val Tyr Phe Asp Lys Val Leu Asn Lys Ala His Gln Ala
                180                 185                 190

    Gly Ile Asp Arg Asp Lys Ile Leu Leu Asp Pro Gly Ile Gly Phe Gly
            195                 200                 205

    Leu Thr Lys Lys Glu Asn Tyr Lys Leu Ile His Ser Val Ala Ser Ile
        210                 215                 220

    His Asp Lys Gly Tyr Pro Val Phe Leu Gly Val Ser Arg Lys Arg Phe
    225                 230                 235                 240

    Leu Val Gly Glu Val Ser Lys Leu Gly Ile Glu Ala Asp Pro Glu Thr
                245                 250                 255

    Gln Ala Gly Phe Leu Asn Arg Asp Leu Ala Ser Ala Ile Ile Thr Ala
                260                 265                 270

    Tyr Ala Ser His Ile Gly Val Asp Tyr Val Arg Val His Ser Leu Asp
            275                 280                 285

    Glu His Lys Ile Ala Thr Thr Ile Thr His Asn Ile Leu Asn Ser Asp
        290                 295                 300

    Ser Leu Asp Asp Gln Ser Phe Asp Gln Tyr Lys Asn
    305                 310                 315


<210> 55
<211> 561
<212> DNA
<213> Alloiococcus otitidis

<220>
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<221> CDS
<222> (28)..(561)
<223>

<400> 55
acaagaacta gacgaaaaat tagaacg ttg gga ata ttt aag cca ata tgt ata        54
                              Met Gly Ile Phe Lys Pro Ile Cys Ile
                              1               5

gga gag ata act atg ata gcc tac gtt tgg gcc caa gat gag caa gga          102
Gly Glu Ile Thr Met Ile Ala Tyr Val Trp Ala Gln Asp Glu Gln Gly
10              15                  20                  25

atc att ggt aaa gac aag gtt ttg cct tgg gaa ttg tcc aat gac tta          150
Ile Ile Gly Lys Asp Lys Val Leu Pro Trp Glu Leu Ser Asn Asp Leu
                30                  35                  40

aag cat ttt aaa aaa gtt aca gaa ggt cac acc atc ctg atg ggc cgg          198
Lys His Phe Lys Lys Val Thr Glu Gly His Thr Ile Leu Met Gly Arg
            45                  50                  55

aag acc ttt gaa gga atg gat aaa aag ccc ctc cct aac cga aaa acc          246
Lys Thr Phe Glu Gly Met Asp Lys Lys Pro Leu Pro Asn Arg Lys Thr
            60                  65                  70

ttg gta ttg acc cgc caa gat gac tac caa gct ggg gac gac cag gtt          294
Leu Val Leu Thr Arg Gln Asp Asp Tyr Gln Ala Gly Asp Asp Gln Val
            75                  80                  85

gaa gtc gtc cac tcc aaa gac cag gcc ttg act tat gcg tca ggt cat          342
Glu Val Val His Ser Lys Asp Gln Ala Leu Thr Tyr Ala Ser Gly His
90              95                  100                 105

ggg gtg gac ctc tat gtg att ggt ggg gcc ggc att ttc gac ttg ttt          390
Gly Val Asp Leu Tyr Val Ile Gly Gly Ala Gly Ile Phe Asp Leu Phe
                110                 115                 120

ctg gac caa gtt gat gtt ctc cac caa aca gtt atc cac gag agc ttt          438
Leu Asp Gln Val Asp Val Leu His Gln Thr Val Ile His Glu Ser Phe
                125                 130                 135

gat ggt gac acc acc atg cca gac att gac tgg gac agc ttt aat cag          486
Asp Gly Asp Thr Thr Met Pro Asp Ile Asp Trp Asp Ser Phe Asn Gln
            140                 145                 150

gtg tct aaa gct tat tat gac cag gct gac ggt cac aac cac tcc cac          534
Val Ser Lys Ala Tyr Tyr Asp Gln Ala Asp Gly His Asn His Ser His
            155                 160                 165

acc att tat gaa tac aga aga aaa taa                                       561
Thr Ile Tyr Glu Tyr Arg Arg Lys
170                 175


<210> 56
<211> 177
<212> PRT
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<213> Alloiococcus otitidis

<400> 56

Met Gly Ile Phe Lys Pro Ile Cys Ile Gly Glu Ile Thr Met Ile Ala
1   5   10   15

Tyr Val Trp Ala Gln Asp Glu Gln Gly Ile Ile Gly Lys Asp Lys Val
              20   25   30

Leu Pro Trp Glu Leu Ser Asn Asp Leu Lys His Phe Lys Lys Val Thr
          35   40   45

Glu Gly His Thr Ile Leu Met Gly Arg Lys Thr Phe Glu Gly Met Asp
      50   55   60

Lys Lys Pro Leu Pro Asn Arg Lys Thr Leu Val Leu Thr Arg Gln Asp
65   70   75   80

Asp Tyr Gln Ala Gly Asp Asp Gln Val Glu Val Val His Ser Lys Asp
                  85   90   95

Gln Ala Leu Thr Tyr Ala Ser Gly His Gly Val Asp Leu Tyr Val Ile
              100   105   110

Gly Gly Ala Gly Ile Phe Asp Leu Phe Leu Asp Gln Val Asp Val Leu
          115   120   125

His Gln Thr Val Ile His Glu Ser Phe Asp Gly Asp Thr Thr Met Pro
      130   135   140

Asp Ile Asp Trp Asp Ser Phe Asn Gln Val Ser Lys Ala Tyr Tyr Asp
145   150   155   160

Gln Ala Asp Gly His Asn His Ser His Thr Ile Tyr Glu Tyr Arg Arg
                  165   170   175

Lys

<210> 57
<211> 1968
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS

<222> (7)..(1968)
<223>

<400> 57
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agagat ttg acg aag gaa tct tac aat gat tca tct ata acc ata ctc        48
       Met Thr Lys Glu Ser Tyr Asn Asp Ser Ser Ile Thr Ile Leu
        1               5                  10

aag ggc tta gac gcc gtt aag aaa aga cca ggc atg tat atc ggg tca        96
Lys Gly Leu Asp Ala Val Lys Lys Arg Pro Gly Met Tyr Ile Gly Ser
15              20                  25                  30

acc gat gcc agg ggt ttg cac cac ctg gtt tat gaa att acc gat aat       144
Thr Asp Ala Arg Gly Leu His His Leu Val Tyr Glu Ile Thr Asp Asn
                35                  40                  45

gct att gat gag gtt ttg gct ggc tac gct gat gaa att gaa gtc aag       192
Ala Ile Asp Glu Val Leu Ala Gly Tyr Ala Asp Glu Ile Glu Val Lys
            50                  55                  60

atc cac acg gac ggc tcg gtt tcg gtc aaa gac aat gga cgg ggc atg       240
Ile His Thr Asp Gly Ser Val Ser Val Lys Asp Asn Gly Arg Gly Met
65                  70                  75

cca acc ggg atg cat gag tca ggc cta ccc acc atc cag gtt atc ttt       288
Pro Thr Gly Met His Glu Ser Gly Leu Pro Thr Ile Gln Val Ile Phe
        80                  85                  90

acc gtc ctc cat gcc ggg gga aaa ttt ggc caa gag ggg gcc tac aag       336
Thr Val Leu His Ala Gly Gly Lys Phe Gly Gln Glu Gly Ala Tyr Lys
95                  100                 105                 110

tca gcc ggt gga ctc cat ggg gtt ggg gcc tcg gtc gtc aac gcc ttg       384
Ser Ala Gly Gly Leu His Gly Val Gly Ala Ser Val Val Asn Ala Leu
                115                 120                 125

tct gat tgg ctc acg gtg ata gtg acc aag gac ggc tat gaa tac cgg       432
Ser Asp Trp Leu Thr Val Ile Val Thr Lys Asp Gly Tyr Glu Tyr Arg
            130                 135                 140

caa gac ttt agc caa gga ggc cag gct aaa gga ggc atc cag aag aga       480
Gln Asp Phe Ser Gln Gly Gly Gln Ala Lys Gly Gly Ile Gln Lys Arg
            145                 150                 155

aaa att aac cag caa aaa tcc agc acc ctg gtc cac ttc aaa ccc tca       528
Lys Ile Asn Gln Gln Lys Ser Ser Thr Leu Val His Phe Lys Pro Ser
160                 165                 170

ggc caa gtc ttt tcg acc acc gaa ttt aac ttt aac acc atc tgt gag       576
Gly Gln Val Phe Ser Thr Thr Glu Phe Asn Phe Asn Thr Ile Cys Glu
175                 180                 185                 190

cgg atg cgg gag tcg gcc ttc ctt gtc aaa ggg acc aag att acc gta       624
Arg Met Arg Glu Ser Ala Phe Leu Val Lys Gly Thr Lys Ile Thr Val
                195                 200                 205

gag gac ctg cgc cag gaa gaa agc cag gtc ttc caa ttt aat gaa gga       672
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```
Glu Asp Leu Arg Gln Glu Glu Ser Gln Val Phe Gln Phe Asn Glu Gly
         210                 215                 220

att aag gcc ttt gtc gac tac tta aat gag ggc aag gat acc ttg agt        720
Ile Lys Ala Phe Val Asp Tyr Leu Asn Glu Gly Lys Asp Thr Leu Ser
         225                 230                 235

cca gta acc tat ttt gaa ggt tct gaa gat gaa att gaa gtt gaa ttt        768
Pro Val Thr Tyr Phe Glu Gly Ser Glu Asp Glu Ile Glu Val Glu Phe
         240                 245                 250

gcc ttc caa tac aat gac ggc tat tcg gag acg gtt ctg agt ttt gtc        816
Ala Phe Gln Tyr Asn Asp Gly Tyr Ser Glu Thr Val Leu Ser Phe Val
255                 260                 265                 270

aac aat gtc cgt acc cgg gat ggg ggc agc cac gaa act gga gct aag        864
Asn Asn Val Arg Thr Arg Asp Gly Gly Ser His Glu Thr Gly Ala Lys
                   275                 280                 285

tca gct att acc aag gct ttc aac gac tat gct agg aaa agt ggc tta        912
Ser Ala Ile Thr Lys Ala Phe Asn Asp Tyr Ala Arg Lys Ser Gly Leu
                   290                 295                 300

ctc aaa gag aaa gac agt aac ttg gaa gga tct gac gtc cgg gaa ggg        960
Leu Lys Glu Lys Asp Ser Asn Leu Glu Gly Ser Asp Val Arg Glu Gly
         305                 310                 315

att gcg gtt gtt tta tcc gtc cgt atc cca gaa gag att ctc caa ttt       1008
Ile Ala Val Val Leu Ser Val Arg Ile Pro Glu Glu Ile Leu Gln Phe
         320                 325                 330

gaa ggc cag acc aag agc aag tta gga act cct caa gcc cgg acc gcc       1056
Glu Gly Gln Thr Lys Ser Lys Leu Gly Thr Pro Gln Ala Arg Thr Ala
335                 340                 345                 350

act gac cag gtt atc tca gaa tcc tta act tac ttc ctg gcc gaa aat       1104
Thr Asp Gln Val Ile Ser Glu Ser Leu Thr Tyr Phe Leu Ala Glu Asn
                   355                 360                 365

ggg gac ttg tct aag caa ctt att cgc aag gcc atc cga gcc cgg tct       1152
Gly Asp Leu Ser Lys Gln Leu Ile Arg Lys Ala Ile Arg Ala Arg Ser
                   370                 375                 380

gcc agg gaa gca gct cgc aag gcc aag gac cag tcc cgg aac tct gct       1200
Ala Arg Glu Ala Ala Arg Lys Ala Lys Asp Gln Ser Arg Asn Ser Ala
         385                 390                 395

tcc aag aaa aaa gtt gaa act ctc ctg tct ggt aag ttg acc cca gct       1248
Ser Lys Lys Lys Val Glu Thr Leu Leu Ser Gly Lys Leu Thr Pro Ala
         400                 405                 410

caa agc aag aac gcc cag aaa aat gaa ctt tac tta gtg gag ggg gat       1296
Gln Ser Lys Asn Ala Gln Lys Asn Glu Leu Tyr Leu Val Glu Gly Asp
415                 420                 425                 430

tcg gct ggt ggg tca gcc aag caa ggt agg gac cgg aaa ttc caa gca       1344
Ser Ala Gly Gly Ser Ala Lys Gln Gly Arg Asp Arg Lys Phe Gln Ala
```

```
                435                  440                  445

att ttg ccc ctg cgt gga aag gtt atc aac aca gaa aaa tct tct ttg      1392
Ile Leu Pro Leu Arg Gly Lys Val Ile Asn Thr Glu Lys Ser Ser Leu
            450                  455                  460

gat gat att tta aaa aat gaa gaa att tct acc atg att tat acc atc      1440
Asp Asp Ile Leu Lys Asn Glu Glu Ile Ser Thr Met Ile Tyr Thr Ile
            465                  470                  475

ggt gca ggt gct ggg cct gag ttt gat att gaa gct gtt aat tac gat      1488
Gly Ala Gly Ala Gly Pro Glu Phe Asp Ile Glu Ala Val Asn Tyr Asp
            480                  485                  490

aag ata gtc att atg act gat gcc gac aca gac ggc gcc cac atc cag      1536
Lys Ile Val Ile Met Thr Asp Ala Asp Thr Asp Gly Ala His Ile Gln
495                  500                  505                  510

gtc ctt ctc ctc acc ttc ttt tac cgg tac atg aaa ccc ctg att gaa      1584
Val Leu Leu Leu Thr Phe Phe Tyr Arg Tyr Met Lys Pro Leu Ile Glu
                515                  520                  525

gca ggg aag gtc tat att gcc cta ccg ccc ttg tat aag ttg acc aaa      1632
Ala Gly Lys Val Tyr Ile Ala Leu Pro Pro Leu Tyr Lys Leu Thr Lys
                530                  535                  540

aag caa gga aag caa gaa aaa aca gcc tat gct tgg act gat gag gag      1680
Lys Gln Gly Lys Gln Glu Lys Thr Ala Tyr Ala Trp Thr Asp Glu Glu
            545                  550                  555

ttg gaa gac ctg gtt aaa gat ttt ggc aaa cac tac act ctc cag cgc      1728
Leu Glu Asp Leu Val Lys Asp Phe Gly Lys His Tyr Thr Leu Gln Arg
            560                  565                  570

tac aag ggt tta ggc gag atg aat gct gac cag ttg tgg gag acc acc      1776
Tyr Lys Gly Leu Gly Glu Met Asn Ala Asp Gln Leu Trp Glu Thr Thr
575                  580                  585                  590

atg gac cca gag acc aga acc ttg atc cgg gtc acc att gaa gac agt      1824
Met Asp Pro Glu Thr Arg Thr Leu Ile Arg Val Thr Ile Glu Asp Ser
                595                  600                  605

gaa aag gct gaa aga cgg gtt tcc acc ttg atg ggg acc aag gtg gat      1872
Glu Lys Ala Glu Arg Arg Val Ser Thr Leu Met Gly Thr Lys Val Asp
                610                  615                  620

cct aga cgg aag tgg att gaa gac cat att gaa ttc agt ctg gca gaa      1920
Pro Arg Arg Lys Trp Ile Glu Asp His Ile Glu Phe Ser Leu Ala Glu
                625                  630                  635

gat ggc agt att tta gag aac aag gtc cta gaa gga gag gcc aag taa      1968
Asp Gly Ser Ile Leu Glu Asn Lys Val Leu Glu Gly Glu Ala Lys
            640                  645                  650
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<210> 58
<211> 653

<212> PRT
<213> Alloiococcus otitidis

<400> 58
Met Thr Lys Glu Ser Tyr Asn Asp Ser Ser Ile Thr Ile Leu Lys Gly
1   5   10   15

Leu Asp Ala Val Lys Lys Arg Pro Gly Met Tyr Ile Gly Ser Thr Asp
            20   25   30

Ala Arg Gly Leu His His Leu Val Tyr Glu Ile Thr Asp Asn Ala Ile
        35   40   45

Asp Glu Val Leu Ala Gly Tyr Ala Asp Glu Ile Glu Val Lys Ile His
    50   55   60

Thr Asp Gly Ser Val Ser Val Lys Asp Asn Gly Arg Gly Met Pro Thr
65   70   75   80

Gly Met His Glu Ser Gly Leu Pro Thr Ile Gln Val Ile Phe Thr Val
                85   90   95

Leu His Ala Gly Gly Lys Phe Gly Gln Glu Gly Ala Tyr Lys Ser Ala
            100   105   110

Gly Gly Leu His Gly Val Gly Ala Ser Val Val Asn Ala Leu Ser Asp
            115   120   125

Trp Leu Thr Val Ile Val Thr Lys Asp Gly Tyr Glu Tyr Arg Gln Asp
    130   135   140

Phe Ser Gln Gly Gly Gln Ala Lys Gly Gly Ile Gln Lys Arg Lys Ile
145   150   155   160

Asn Gln Gln Lys Ser Ser Thr Leu Val His Phe Lys Pro Ser Gly Gln
            165   170   175

Val Phe Ser Thr Thr Glu Phe Asn Phe Asn Thr Ile Cys Glu Arg Met
            180   185   190

Arg Glu Ser Ala Phe Leu Val Lys Gly Thr Lys Ile Thr Val Glu Asp
        195   200   205

Leu Arg Gln Glu Glu Ser Gln Val Phe Gln Phe Asn Glu Gly Ile Lys

                    210   215   220

Ala Phe Val Asp Tyr Leu Asn Glu Gly Lys Asp Thr Leu Ser Pro Val
225   230   235   240

Thr Tyr Phe Glu Gly Ser Glu Asp Glu Ile Glu Val Glu Phe Ala Phe
                    245   250   255

Gln Tyr Asn Asp Gly Tyr Ser Glu Thr Val Leu Ser Phe Val Asn Asn
                    260   265   270

Val Arg Thr Arg Asp Gly Gly Ser His Glu Thr Gly Ala Lys Ser Ala
                    275   280   285

Ile Thr Lys Ala Phe Asn Asp Tyr Ala Arg Lys Ser Gly Leu Leu Lys
                    290   295   300

Glu Lys Asp Ser Asn Leu Glu Gly Ser Asp Val Arg Glu Gly Ile Ala
305   310   315   320

Val Val Leu Ser Val Arg Ile Pro Glu Glu Ile Leu Gln Phe Glu Gly
                    325   330   335

Gln Thr Lys Ser Lys Leu Gly Thr Pro Gln Ala Arg Thr Ala Thr Asp
                    340   345   350

Gln Val Ile Ser Glu Ser Leu Thr Tyr Phe Leu Ala Glu Asn Gly Asp
                    355   360   365

Leu Ser Lys Gln Leu Ile Arg Lys Ala Ile Arg Ala Arg Ser Ala Arg
370   375   380

Glu Ala Ala Arg Lys Ala Lys Asp Gln Ser Arg Asn Ser Ala Ser Lys
385   390   395   400

Lys Lys Val Glu Thr Leu Leu Ser Gly Lys Leu Thr Pro Ala Gln Ser
                    405   410   415

Lys Asn Ala Gln Lys Asn Glu Leu Tyr Leu Val Glu Gly Asp Ser Ala
                    420   425   430

Gly Gly Ser Ala Lys Gln Gly Arg Asp Arg Lys Phe Gln Ala Ile Leu
                    435   440   445

```
Pro Leu Arg Gly Lys Val Ile Asn Thr Glu Lys Ser Ser Leu Asp Asp
    450             455             460

Ile Leu Lys Asn Glu Glu Ile Ser Thr Met Ile Tyr Thr Ile Gly Ala
465             470             475             480

Gly Ala Gly Pro Glu Phe Asp Ile Glu Ala Val Asn Tyr Asp Lys Ile
                485             490             495

Val Ile Met Thr Asp Ala Asp Thr Asp Gly Ala His Ile Gln Val Leu
            500             505             510

Leu Leu Thr Phe Phe Tyr Arg Tyr Met Lys Pro Leu Ile Glu Ala Gly
            515             520             525

Lys Val Tyr Ile Ala Leu Pro Pro Leu Tyr Lys Leu Thr Lys Lys Gln
    530             535             540

Gly Lys Gln Glu Lys Thr Ala Tyr Ala Trp Thr Asp Glu Glu Leu Glu
545             550             555             560

Asp Leu Val Lys Asp Phe Gly Lys His Tyr Thr Leu Gln Arg Tyr Lys
                565             570             575

Gly Leu Gly Glu Met Asn Ala Asp Gln Leu Trp Glu Thr Thr Met Asp
            580             585             590

Pro Glu Thr Arg Thr Leu Ile Arg Val Thr Ile Glu Asp Ser Glu Lys
            595             600             605

Ala Glu Arg Arg Val Ser Thr Leu Met Gly Thr Lys Val Asp Pro Arg
    610             615             620

Arg Lys Trp Ile Glu Asp His Ile Glu Phe Ser Leu Ala Glu Asp Gly
625             630             635             640

Ser Ile Leu Glu Asn Lys Val Leu Glu Gly Glu Ala Lys
            645             650
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<210> 59
<211> 2463
<212> DNA

<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (4)..(2463)
<223>

<400> 59
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att atg gca gga gac caa gag acc agt aaa ata caa gaa tta acc tta      48
    Met Ala Gly Asp Gln Glu Thr Ser Lys Ile Gln Glu Leu Thr Leu
    1               5                  10                  15

gaa gat gtc atg ggg gac cgg ttc ggc cgg tat tcc aag tac att ata      96
Glu Asp Val Met Gly Asp Arg Phe Gly Arg Tyr Ser Lys Tyr Ile Ile
                20                  25                  30

cag gaa agg gcc cta ccg gac ttg cgg gac ggt tta aaa ccg gtc caa     144
Gln Glu Arg Ala Leu Pro Asp Leu Arg Asp Gly Leu Lys Pro Val Gln
            35                  40                  45

aga cgg atc ctc tat gcc atg cac cag gac aaa aac acc tat gac aag     192
Arg Arg Ile Leu Tyr Ala Met His Gln Asp Lys Asn Thr Tyr Asp Lys
        50                  55                  60

gct tac cgg aag tcg gcc aag acg gtg gga aat gtc ata ggg aac tac     240
Ala Tyr Arg Lys Ser Ala Lys Thr Val Gly Asn Val Ile Gly Asn Tyr
    65                  70                  75

cac ccc cat ggc gac aca tcc gtt tac gat gcc atg gtt agg ctc agt     288
His Pro His Gly Asp Thr Ser Val Tyr Asp Ala Met Val Arg Leu Ser
80                  85                  90                  95

cag cct tgg aag atg cgc cat cct ttg gtt gat atg cac ggg aac aag     336
Gln Pro Trp Lys Met Arg His Pro Leu Val Asp Met His Gly Asn Lys
                100                 105                 110

ggg agc atg gac ggg gac cca cca gct gcc atg cgg tac acc gaa gcc     384
Gly Ser Met Asp Gly Asp Pro Pro Ala Ala Met Arg Tyr Thr Glu Ala
            115                 120                 125

cgt ctg tct aaa att gct tcc gac ctc ctg gct gat att gat aag gag     432
Arg Leu Ser Lys Ile Ala Ser Asp Leu Leu Ala Asp Ile Asp Lys Glu
        130                 135                 140

acg gtg gac cat gtc tta aac ttt gat gac acg acc gag gag ccc acc     480
Thr Val Asp His Val Leu Asn Phe Asp Asp Thr Thr Glu Glu Pro Thr
    145                 150                 155

gtc tta ccc gcc cgt ttt ccc aac ctc ttg gtc aat ggg gct agc ggg     528
Val Leu Pro Ala Arg Phe Pro Asn Leu Leu Val Asn Gly Ala Ser Gly
160                 165                 170                 175

att tca gcc ggt tat gct act gac ata ccg ccc cat aat ttg agc gag     576
Ile Ser Ala Gly Tyr Ala Thr Asp Ile Pro Pro His Asn Leu Ser Glu
                180                 185                 190

gtg att gat gcc acc atc cac tta atc aac cac ccc aat gca agg ctg     624
```

```
                    Val Ile Asp Ala Thr Ile His Leu Ile Asn His Pro Asn Ala Arg Leu
                                195             200             205

gag act ttg atg gac tat att caa gga cca gac ttt ccg act ggg ggg      672
Glu Thr Leu Met Asp Tyr Ile Gln Gly Pro Asp Phe Pro Thr Gly Gly
            210             215             220

att atc caa ggt aaa agt ggc ctg aag aaa gcc tac caa acg ggc aag      720
Ile Ile Gln Gly Lys Ser Gly Leu Lys Lys Ala Tyr Gln Thr Gly Lys
            225             230             235

gga aaa att atc atc cgg gcc aaa gca gat att gag gcc atc cgg ggt      768
Gly Lys Ile Ile Ile Arg Ala Lys Ala Asp Ile Glu Ala Ile Arg Gly
240             245             250             255

ggc aaa tcc caa att gtc atc agt caa att cct tat gag gtc aac aag      816
Gly Lys Ser Gln Ile Val Ile Ser Gln Ile Pro Tyr Glu Val Asn Lys
            260             265             270

gca agg ttg gtc caa aaa att gac gac atc cgg att aac aaa aaa atc      864
Ala Arg Leu Val Gln Lys Ile Asp Asp Ile Arg Ile Asn Lys Lys Ile
            275             280             285

gac ggc att gcc gat gtc cgg gat gaa agt gac cgg tct ggc ttg cgg      912
Asp Gly Ile Ala Asp Val Arg Asp Glu Ser Asp Arg Ser Gly Leu Arg
            290             295             300

att gtg gtc gaa acc aaa aaa gat ggt gat ggg gaa ggg atc tta acc      960
Ile Val Val Glu Thr Lys Lys Asp Gly Asp Gly Glu Gly Ile Leu Thr
            305             310             315

tac ctg ctg aaa aac acc gac ctc cag gta act tat aac tta aat atg      1008
Tyr Leu Leu Lys Asn Thr Asp Leu Gln Val Thr Tyr Asn Leu Asn Met
320             325             330             335

gta gcc att gat aaa aaa cga ccc cag caa gtc tcc ctc aag caa atc      1056
Val Ala Ile Asp Lys Lys Arg Pro Gln Gln Val Ser Leu Lys Gln Ile
            340             345             350

tta tct tct tac ttg gac cac aag cgg aca gtg gtt caa aac cgg acc      1104
Leu Ser Ser Tyr Leu Asp His Lys Arg Thr Val Val Gln Asn Arg Thr
            355             360             365

cgt tac ctc tta gcc aag gcc aag gac cgc cag cac att gtc caa ggc      1152
Arg Tyr Leu Leu Ala Lys Ala Lys Asp Arg Gln His Ile Val Gln Gly
            370             375             380

ctt atc aag gcc att tca atc ctg gat gac ttg atc caa acc atc cgg      1200
Leu Ile Lys Ala Ile Ser Ile Leu Asp Asp Leu Ile Gln Thr Ile Arg
            385             390             395

gcc agt gaa aac aag gcc aat gcc aag gaa aat att atc cag gct tat      1248
Ala Ser Glu Asn Lys Ala Asn Ala Lys Glu Asn Ile Ile Gln Ala Tyr
400             405             410             415

ggt ttt agc caa gac caa gcc gaa gcc att gtc tcc ctc cag ctt tac      1296
Gly Phe Ser Gln Asp Gln Ala Glu Ala Ile Val Ser Leu Gln Leu Tyr
```

                420   425   430

cgc ttg acc aat aca gat ata aag gac tta caa gca gaa gcc aaa gac   1344
Arg Leu Thr Asn Thr Asp Ile Lys Asp Leu Gln Ala Glu Ala Lys Asp
            435   440   445

tta gcc caa gcc atc ctg acc tac cag gac ctc tta acc aac aag gcc   1392
Leu Ala Gln Ala Ile Leu Thr Tyr Gln Asp Leu Leu Thr Asn Lys Ala
            450   455   460

agc ctg gat gct ttg atg aaa gaa gaa ttg aaa gaa gtc aaa caa gca   1440
Ser Leu Asp Ala Leu Met Lys Glu Glu Leu Lys Glu Val Lys Gln Ala
            465   470   475

tat ggg gag gac cgg cta acc cag gtc caa gac aag atc gaa aaa cta   1488
Tyr Gly Glu Asp Arg Leu Thr Gln Val Gln Asp Lys Ile Glu Lys Leu
480   485   490   495

gaa ata gaa acc caa gtc ctg gtc agt gaa gaa gac gtc atg gtt acc   1536
Glu Ile Glu Thr Gln Val Leu Val Ser Glu Glu Asp Val Met Val Thr
                500   505   510

gtc acc cag gga ggt tac ttg aag cgg acc tcc atc cgg tct tac aag   1584
Val Thr Gln Gly Gly Tyr Leu Lys Arg Thr Ser Ile Arg Ser Tyr Lys
                515   520   525

gct tcc caa gtg gag gaa ttg ggc cgg cga gaa gac gac ttg gtc atc   1632
Ala Ser Gln Val Glu Glu Leu Gly Arg Arg Glu Asp Asp Leu Val Ile
                530   535   540

ttt atg caa gag ttg tca acc cta gac caa ctc ctt att ttc acc tcg   1680
Phe Met Gln Glu Leu Ser Thr Leu Asp Gln Leu Leu Ile Phe Thr Ser
                545   550   555

aaa ggc aat gtg gtc aac cga cca gtc cat gaa tta ccg gac atc aag   1728
Lys Gly Asn Val Val Asn Arg Pro Val His Glu Leu Pro Asp Ile Lys
560   565   570   575

tgg aag gat att gga gag cac ttg tca agg acc atc ccc ctt gga gag   1776
Trp Lys Asp Ile Gly Glu His Leu Ser Arg Thr Ile Pro Leu Gly Glu
                580   585   590

gac gag gaa ttg att aag gtg tac cct tat cgg gaa tta gat gcc ggc   1824
Asp Glu Glu Leu Ile Lys Val Tyr Pro Tyr Arg Glu Leu Asp Ala Gly
                595   600   605

aag cgc tat gtc ttt atc act cga gat ggc tat atc aaa caa agt cca   1872
Lys Arg Tyr Val Phe Ile Thr Arg Asp Gly Tyr Ile Lys Gln Ser Pro
                610   615   620

gag acg gaa ttt gag ccc aaa cga act tac aag tct cgg gct tca act   1920
Glu Thr Glu Phe Glu Pro Lys Arg Thr Tyr Lys Ser Arg Ala Ser Thr
                625   630   635

gcc att aaa tta aaa tca gac caa gat aga ctc cag gca gtc tac tat   1968
Ala Ile Lys Leu Lys Ser Asp Gln Asp Arg Leu Gln Ala Val Tyr Tyr
640   645   650   655

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att cct gac caa gaa gat tac gat gta ttc cta gcc agc tac aag ggc    2016
Ile Pro Asp Gln Glu Asp Tyr Asp Val Phe Leu Ala Ser Tyr Lys Gly
            660             665             670

tac ggg ctc aag tat gga cta gaa gaa gtg tca gaa gta ggg gcc cag    2064
Tyr Gly Leu Lys Tyr Gly Leu Glu Glu Val Ser Glu Val Gly Ala Gln
            675             680             685

gct gca ggc gtc aag tcc atg aac ctg aaa gag ggg gac cat gtc caa    2112
Ala Ala Gly Val Lys Ser Met Asn Leu Lys Glu Gly Asp His Val Gln
            690             695             700

gat ggt ttg gtc ttt aag cgt aag cag ttc caa gaa gcc ttg ttc att    2160
Asp Gly Leu Val Phe Lys Arg Lys Gln Phe Gln Glu Ala Leu Phe Ile
            705             710             715

acc cag cga gcc agt gtt aag aaa atg gcc ctc cat gac ttt gac cgg    2208
Thr Gln Arg Ala Ser Val Lys Lys Met Ala Leu His Asp Phe Asp Arg
720             725             730             735

act tca cgg gcc aag cgg ggt tta caa atc ctc aga gaa ctg aag cga    2256
Thr Ser Arg Ala Lys Arg Gly Leu Gln Ile Leu Arg Glu Leu Lys Arg
            740             745             750

aac ccc cac cga atc cag ttt atg atc gga att tca caa aat aaa ttc    2304
Asn Pro His Arg Ile Gln Phe Met Ile Gly Ile Ser Gln Asn Lys Phe
            755             760             765

ctg gtc aat ctc cta act gat aca aaa aaa cta gta cag ata aac cca    2352
Leu Val Asn Leu Leu Thr Asp Thr Lys Lys Leu Val Gln Ile Asn Pro
            770             775             780

gat gac tat aca gtt tca aac cgc cat aac aat ggg tct ttt gtc ctg    2400
Asp Asp Tyr Thr Val Ser Asn Arg His Asn Asn Gly Ser Phe Val Leu
            785             790             795

gac aca agc cga gat ggc aag cct gtt tct tac tat tta agt gat aac    2448
Asp Thr Ser Arg Asp Gly Lys Pro Val Ser Tyr Tyr Leu Ser Asp Asn
800             805             810             815

gat tct cac ttg taa                                                2463
Asp Ser His Leu


<210> 60
<211> 819
<212> PRT
<213> Alloiococcus otitidis

<400> 60
Met Ala Gly Asp Gln Glu Thr Ser Lys Ile Gln Glu Leu Thr Leu Glu
1               5               10              15


Asp Val Met Gly Asp Arg Phe Gly Arg Tyr Ser Lys Tyr Ile Ile Gln
            20              25              30
```

Glu Arg Ala Leu Pro Asp Leu Arg Asp Gly Leu Lys Pro Val Gln Arg
        35   40   45

Arg Ile Leu Tyr Ala Met His Gln Asp Lys Asn Thr Tyr Asp Lys Ala
        50   55   60

Tyr Arg Lys Ser Ala Lys Thr Val Gly Asn Val Ile Gly Asn Tyr His
65   70   75   80

Pro His Gly Asp Thr Ser Val Tyr Asp Ala Met Val Arg Leu Ser Gln
                85   90   95

Pro Trp Lys Met Arg His Pro Leu Val Asp Met His Gly Asn Lys Gly
            100   105   110

Ser Met Asp Gly Asp Pro Pro Ala Ala Met Arg Tyr Thr Glu Ala Arg
            115   120   125

Leu Ser Lys Ile Ala Ser Asp Leu Leu Ala Asp Ile Asp Lys Glu Thr
        130   135   140

Val Asp His Val Leu Asn Phe Asp Asp Thr Thr Glu Glu Pro Thr Val
145   150   155   160

Leu Pro Ala Arg Phe Pro Asn Leu Leu Val Asn Gly Ala Ser Gly Ile
                165   170   175

Ser Ala Gly Tyr Ala Thr Asp Ile Pro Pro His Asn Leu Ser Glu Val
            180   185   190

Ile Asp Ala Thr Ile His Leu Ile Asn His Pro Asn Ala Arg Leu Glu
        195   200   205

Thr Leu Met Asp Tyr Ile Gln Gly Pro Asp Phe Pro Thr Gly Gly Ile
        210   215   220

Ile Gln Gly Lys Ser Gly Leu Lys Lys Ala Tyr Gln Thr Gly Lys Gly
225   230   235   240

Lys Ile Ile Ile Arg Ala Lys Ala Asp Ile Glu Ala Ile Arg Gly Gly
                245   250   255

```
Lys Ser Gln Ile Val Ile Ser Gln Ile Pro Tyr Glu Val Asn Lys Ala
        260             265             270

Arg Leu Val Gln Lys Ile Asp Asp Ile Arg Ile Asn Lys Lys Ile Asp
        275             280             285

Gly Ile Ala Asp Val Arg Asp Glu Ser Asp Arg Ser Gly Leu Arg Ile
    290             295             300

Val Val Glu Thr Lys Lys Asp Gly Asp Gly Glu Gly Ile Leu Thr Tyr
305             310             315             320

Leu Leu Lys Asn Thr Asp Leu Gln Val Thr Tyr Asn Leu Asn Met Val
            325             330             335

Ala Ile Asp Lys Lys Arg Pro Gln Gln Val Ser Leu Lys Gln Ile Leu
            340             345             350

Ser Ser Tyr Leu Asp His Lys Arg Thr Val Val Gln Asn Arg Thr Arg
        355             360             365

Tyr Leu Leu Ala Lys Ala Lys Asp Arg Gln His Ile Val Gln Gly Leu
    370             375             380

Ile Lys Ala Ile Ser Ile Leu Asp Asp Leu Ile Gln Thr Ile Arg Ala
385             390             395             400

Ser Glu Asn Lys Ala Asn Ala Lys Glu Asn Ile Ile Gln Ala Tyr Gly
            405             410             415

Phe Ser Gln Asp Gln Ala Glu Ala Ile Val Ser Leu Gln Leu Tyr Arg
            420             425             430

Leu Thr Asn Thr Asp Ile Lys Asp Leu Gln Ala Glu Ala Lys Asp Leu
        435             440             445

Ala Gln Ala Ile Leu Thr Tyr Gln Asp Leu Leu Thr Asn Lys Ala Ser
    450             455             460

Leu Asp Ala Leu Met Lys Glu Glu Leu Lys Glu Val Lys Gln Ala Tyr
465             470             475             480
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Gly Glu Asp Arg Leu Thr Gln Val Gln Asp Lys Ile Glu Lys Leu Glu
          485   490   495

Ile Glu Thr Gln Val Leu Val Ser Glu Glu Asp Val Met Val Thr Val
          500   505   510

Thr Gln Gly Gly Tyr Leu Lys Arg Thr Ser Ile Arg Ser Tyr Lys Ala
          515   520   525

Ser Gln Val Glu Glu Leu Gly Arg Arg Glu Asp Asp Leu Val Ile Phe
    530   535   540

Met Gln Glu Leu Ser Thr Leu Asp Gln Leu Leu Ile Phe Thr Ser Lys
545   550   555   560

Gly Asn Val Val Asn Arg Pro Val His Glu Leu Pro Asp Ile Lys Trp
          565   570   575

Lys Asp Ile Gly Glu His Leu Ser Arg Thr Ile Pro Leu Gly Glu Asp
          580   585   590

Glu Glu Leu Ile Lys Val Tyr Pro Tyr Arg Glu Leu Asp Ala Gly Lys
     595   600   605

Arg Tyr Val Phe Ile Thr Arg Asp Gly Tyr Ile Lys Gln Ser Pro Glu
    610   615   620

Thr Glu Phe Glu Pro Lys Arg Thr Tyr Lys Ser Arg Ala Ser Thr Ala
625   630   635   640

Ile Lys Leu Lys Ser Asp Gln Asp Arg Leu Gln Ala Val Tyr Tyr Ile
          645   650   655

Pro Asp Gln Glu Asp Tyr Asp Val Phe Leu Ala Ser Tyr Lys Gly Tyr
          660   665   670

Gly Leu Lys Tyr Gly Leu Glu Glu Val Ser Glu Val Gly Ala Gln Ala
          675   680   685

Ala Gly Val Lys Ser Met Asn Leu Lys Glu Gly Asp His Val Gln Asp
     690   695   700

Gly Leu Val Phe Lys Arg Lys Gln Phe Gln Glu Ala Leu Phe Ile Thr

705   710   715   720

```
Gln Arg Ala Ser Val Lys Lys Met Ala Leu His Asp Phe Asp Arg Thr
                725             730             735

Ser Arg Ala Lys Arg Gly Leu Gln Ile Leu Arg Glu Leu Lys Arg Asn
            740             745             750

Pro His Arg Ile Gln Phe Met Ile Gly Ile Ser Gln Asn Lys Phe Leu
        755             760             765

Val Asn Leu Leu Thr Asp Thr Lys Lys Leu Val Gln Ile Asn Pro Asp
    770             775             780

Asp Tyr Thr Val Ser Asn Arg His Asn Asn Gly Ser Phe Val Leu Asp
785             790             795             800

Thr Ser Arg Asp Gly Lys Pro Val Ser Tyr Tyr Leu Ser Asp Asn Asp
            805             810             815

Ser His Leu
```

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<210> 61
<211> 1113
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (4)..(1113)
<223>

<400> 61
tta gtg gtt gag aca aaa tca aaa cta gaa aat gca gta aac acc ctc      48
    Met Val Glu Thr Lys Ser Lys Leu Glu Asn Ala Val Asn Thr Leu
    1             5               10              15

att aaa gac ttg aaa aat aaa aaa gag tcg acc att tct tat att gac      96
Ile Lys Asp Leu Lys Asn Lys Lys Glu Ser Thr Ile Ser Tyr Ile Asp
            20              25              30

ctc agc aac aaa att gct gaa ccc ttc gaa ctt gaa agt gaa gcc atg     144
Leu Ser Asn Lys Ile Ala Glu Pro Phe Glu Leu Glu Ser Glu Ala Met
        35              40              45

gac aag tta atc cag caa tta gaa gat gat ggg att ggt gta gtt gac     192
Asp Lys Leu Ile Gln Gln Leu Glu Asp Asp Gly Ile Gly Val Val Asp
        50              55              60
```

```
caa gac ggt aat ccc ttg gcc aag caa cta gcc aag cag gaa gaa gaa      240
Gln Asp Gly Asn Pro Leu Ala Lys Gln Leu Ala Lys Gln Glu Glu Glu
    65              70              75


gca gaa aaa gcc aag gat gaa gaa atg ata gcc cca cct ggg gtt aaa      288
Ala Glu Lys Ala Lys Asp Glu Glu Met Ile Ala Pro Pro Gly Val Lys
80              85              90              95


att aac gac cct gtc cgg atg tac cta aaa gaa att ggc cgg gta gat      336
Ile Asn Asp Pro Val Arg Met Tyr Leu Lys Glu Ile Gly Arg Val Asp
                100             105             110


ctt tta gat gct gaa gaa gaa gtg gcc cta gcc aag cgg att gaa gaa      384
Leu Leu Asp Ala Glu Glu Glu Val Ala Leu Ala Lys Arg Ile Glu Glu
                115             120             125


ggc gat gaa atc gct aaa caa gaa cta gct gag gct aac ttg aga ctg      432
Gly Asp Glu Ile Ala Lys Gln Glu Leu Ala Glu Ala Asn Leu Arg Leu
            130             135             140


gtt gtc tct att gct aaa cgg tac gtt ggc cgg ggc atg agc ttt ttg      480
Val Val Ser Ile Ala Lys Arg Tyr Val Gly Arg Gly Met Ser Phe Leu
    145             150             155


gac ttg atc cag gaa ggg aat atg ggg cta atg aag gca gtt gaa aaa      528
Asp Leu Ile Gln Glu Gly Asn Met Gly Leu Met Lys Ala Val Glu Lys
160             165             170             175


ttt gac tac gaa aaa ggt ttc aaa ttt tca acc tat gcc acc tgg tgg      576
Phe Asp Tyr Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trp
                180             185             190


atc cgt caa gcc atc act cgg gcc att gcc gac caa gcc cga acc atc      624
Ile Arg Gln Ala Ile Thr Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile
            195             200             205


cgg att ccg gtc cac atg gtc gaa act att aac aag ctg gtc cga atc      672
Arg Ile Pro Val His Met Val Glu Thr Ile Asn Lys Leu Val Arg Ile
        210             215             220


cag cgg cag ctc cta caa gaa cta ggc cgg gaa cca acc cca gaa gaa      720
Gln Arg Gln Leu Leu Gln Glu Leu Gly Arg Glu Pro Thr Pro Glu Glu
    225             230             235


att ggg gca gag atg gat ttg cca acc gaa aaa gtc aga gat att ttg      768
Ile Gly Ala Glu Met Asp Leu Pro Thr Glu Lys Val Arg Asp Ile Leu
240             245             250             255


aaa att tcc caa gaa ccc gtc tcc ctt gaa acc cca att ggg gaa gaa      816
Lys Ile Ser Gln Glu Pro Val Ser Leu Glu Thr Pro Ile Gly Glu Glu
                260             265             270


gaa gat tcc cac ctg gga gac ttt att gaa gat gat ggg gcc ttg tcg      864
Glu Asp Ser His Leu Gly Asp Phe Ile Glu Asp Asp Gly Ala Leu Ser
            275             280             285


cca tct gat aat gca gct tat gag ctg ttg aaa ggg gaa ctc aaa gga      912
```

```
Pro Ser Asp Asn Ala Ala Tyr Glu Leu Leu Lys Gly Glu Leu Lys Gly
    290             295             300

gtc tta gac acc cta act gac cgg gaa gaa aat gtc ttg cgc ctc cgt     960
Val Leu Asp Thr Leu Thr Asp Arg Glu Glu Asn Val Leu Arg Leu Arg
    305             310             315

ttt ggc cta gat gat ggc cgt caa cgt act tta gaa gat gtc ggt aag    1008
Phe Gly Leu Asp Asp Gly Arg Gln Arg Thr Leu Glu Asp Val Gly Lys
320             325             330             335

gtc ttt ggg gtc acc cgg gag cgg atc cgt caa att gaa gcg aag gcc    1056
Val Phe Gly Val Thr Arg Glu Arg Ile Arg Gln Ile Glu Ala Lys Ala
                340             345             350

ctc cgc aaa ctc cgc cac cct agc cgg tcc aaa caa tta aaa gac ttt    1104
Leu Arg Lys Leu Arg His Pro Ser Arg Ser Lys Gln Leu Lys Asp Phe
                355             360             365

tta gaa tag                                                         1113
Leu Glu


<210> 62
<211> 369
<212> PRT
<213> Alloiococcus otitidis

<400> 62
Met Val Glu Thr Lys Ser Lys Leu Glu Asn Ala Val Asn Thr Leu Ile
1               5               10              15


Lys Asp Leu Lys Asn Lys Lys Glu Ser Thr Ile Ser Tyr Ile Asp Leu
        20              25              30


Ser Asn Lys Ile Ala Glu Pro Phe Glu Leu Glu Ser Glu Ala Met Asp
        35              40              45


Lys Leu Ile Gln Gln Leu Glu Asp Asp Gly Ile Gly Val Val Asp Gln
    50              55              60


Asp Gly Asn Pro Leu Ala Lys Gln Leu Ala Lys Gln Glu Glu Glu Ala
65              70              75              80


Glu Lys Ala Lys Asp Glu Glu Met Ile Ala Pro Pro Gly Val Lys Ile
            85              90              95


Asn Asp Pro Val Arg Met Tyr Leu Lys Glu Ile Gly Arg Val Asp Leu
            100             105             110
```

Leu Asp Ala Glu Glu Glu Val Ala Leu Ala Lys Arg Ile Glu Glu Gly
        115   120   125

Asp Glu Ile Ala Lys Gln Glu Leu Ala Glu Ala Asn Leu Arg Leu Val
        130   135   140

Val Ser Ile Ala Lys Arg Tyr Val Gly Arg Gly Met Ser Phe Leu Asp
145   150   155   160

Leu Ile Gln Glu Gly Asn Met Gly Leu Met Lys Ala Val Glu Lys Phe
                165   170   175

Asp Tyr Glu Lys Gly Phe Lys Phe Ser Thr Tyr Ala Thr Trp Trp Ile
            180   185   190

Arg Gln Ala Ile Thr Arg Ala Ile Ala Asp Gln Ala Arg Thr Ile Arg
        195   200   205

Ile Pro Val His Met Val Glu Thr Ile Asn Lys Leu Val Arg Ile Gln
    210   215   220

Arg Gln Leu Leu Gln Glu Leu Gly Arg Glu Pro Thr Pro Glu Glu Ile
225   230   235   240

Gly Ala Glu Met Asp Leu Pro Thr Glu Lys Val Arg Asp Ile Leu Lys
                245   250   255

Ile Ser Gln Glu Pro Val Ser Leu Glu Thr Pro Ile Gly Glu Glu Glu
                260   265   270

Asp Ser His Leu Gly Asp Phe Ile Glu Asp Asp Gly Ala Leu Ser Pro
        275   280   285

Ser Asp Asn Ala Ala Tyr Glu Leu Leu Lys Gly Glu Leu Lys Gly Val
    290   295   300

Leu Asp Thr Leu Thr Asp Arg Glu Glu Asn Val Leu Arg Leu Arg Phe
305   310   315   320

Gly Leu Asp Asp Gly Arg Gln Arg Thr Leu Glu Asp Val Gly Lys Val
                325   330   335

Phe Gly Val Thr Arg Glu Arg Ile Arg Gln Ile Glu Ala Lys Ala Leu

```
              340                  345                  350


Arg Lys Leu Arg His Pro Ser Arg Ser Lys Gln Leu Lys Asp Phe Leu
        355                  360                  365


Glu


<210> 63
<211> 1854
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (1)..(1854)
<223>

<400> 63
atg gtt aga ata cct gaa gag acc att aat caa ata cga agc cag gca      48
Met Val Arg Ile Pro Glu Glu Thr Ile Asn Gln Ile Arg Ser Gln Ala
1               5                  10                  15

gat att gtc gat gtc att ggc caa tac ttg gac tta aac aag tct ggg      96
Asp Ile Val Asp Val Ile Gly Gln Tyr Leu Asp Leu Asn Lys Ser Gly
                20                  25                  30

gcc aat tac ttt gcc cac tgc ccc ttc cat gaa gac agc acg cct tct     144
Ala Asn Tyr Phe Ala His Cys Pro Phe His Glu Asp Ser Thr Pro Ser
            35                  40                  45

ttt tcg gtc aac aga gac aag caa att tat aag tgc ttt tct tgc aaa     192
Phe Ser Val Asn Arg Asp Lys Gln Ile Tyr Lys Cys Phe Ser Cys Lys
        50                  55                  60

cga ggt ggc agt gtc ttt agc ttt ata caa gag aag gag gga ctt tcc     240
Arg Gly Gly Ser Val Phe Ser Phe Ile Gln Glu Lys Glu Gly Leu Ser
65                  70                  75                  80

ttc cca gaa tcg gtt ctt aaa gtg gca gac tta gct aat gtg gac ctt     288
Phe Pro Glu Ser Val Leu Lys Val Ala Asp Leu Ala Asn Val Asp Leu
                85                  90                  95

gat ccg gcc tta aaa gaa gct gtc caa ggc caa cct gac aaa gcc gat     336
Asp Pro Ala Leu Lys Glu Ala Val Gln Gly Gln Pro Asp Lys Ala Asp
            100                 105                 110

tct ccc tac cga gac ctc tat acc atc cat gac cag gcc aag gac tac     384
Ser Pro Tyr Arg Asp Leu Tyr Thr Ile His Asp Gln Ala Lys Asp Tyr
            115                 120                 125

tac cag tat atc ctc tta aag gcc cag gtg gga gaa gtt gct tac gac     432
Tyr Gln Tyr Ile Leu Leu Lys Ala Gln Val Gly Glu Val Ala Tyr Asp
        130                 135                 140
```

```
tat ctc cag aat cgt ggg att tcc aga gag gtg atg gaa gag ttc gaa        480
Tyr Leu Gln Asn Arg Gly Ile Ser Arg Glu Val Met Glu Glu Phe Glu
145                 150                 155                 160

ctg ggt tat tct ccc agc caa agg gag tcg ctc cac ctt tat ttg cag        528
Leu Gly Tyr Ser Pro Ser Gln Arg Glu Ser Leu His Leu Tyr Leu Gln
                165                 170                 175

tcc caa gac cag gcg gac ttg aca gat gac tta ctg gaa gaa acc ggc        576
Ser Gln Asp Gln Ala Asp Leu Thr Asp Asp Leu Leu Glu Glu Thr Gly
            180                 185                 190

ctt ttt tcc aaa aga gaa gtg gaa agt gat agt ttt aaa gac cgc ttt        624
Leu Phe Ser Lys Arg Glu Val Glu Ser Asp Ser Phe Lys Asp Arg Phe
            195                 200                 205

gcc aag cgg atc atc ttc ccc tta aag aac tta caa ggg cag acg gtg        672
Ala Lys Arg Ile Ile Phe Pro Leu Lys Asn Leu Gln Gly Gln Thr Val
    210                 215                 220

ggc ttt tcg ggc cgg tat ttc caa gat gag cct aac cag gac ttc cat        720
Gly Phe Ser Gly Arg Tyr Phe Gln Asp Glu Pro Asn Gln Asp Phe His
225                 230                 235                 240

cat gcc aag tat tta aac agt cca gaa acc aaa ata ttc aat aaa cgg        768
His Ala Lys Tyr Leu Asn Ser Pro Glu Thr Lys Ile Phe Asn Lys Arg
                245                 250                 255

cgg acc ctc ttt aac tac cac cag gcc aag gcc tac att cgt cgg gcc        816
Arg Thr Leu Phe Asn Tyr His Gln Ala Lys Ala Tyr Ile Arg Arg Ala
                260                 265                 270

aag gaa gtt gtc tta ttc gaa ggt tac atg gat gtg att gct gct tgg        864
Lys Glu Val Val Leu Phe Glu Gly Tyr Met Asp Val Ile Ala Ala Trp
            275                 280                 285

caa gcg ggg gtc aaa aat ggc tta gct tcc atg ggg acc agt ata aca        912
Gln Ala Gly Val Lys Asn Gly Leu Ala Ser Met Gly Thr Ser Ile Thr
            290                 295                 300

gct gac caa gtc cag acc atg caa agg att gct gac acc tta gtc ttg        960
Ala Asp Gln Val Gln Thr Met Gln Arg Ile Ala Asp Thr Leu Val Leu
305                 310                 315                 320

gcc ttt gac ggg gat gaa gct ggc ctt gaa tcc agc aaa aag atc ctg       1008
Ala Phe Asp Gly Asp Glu Ala Gly Leu Glu Ser Ser Lys Lys Ile Leu
                325                 330                 335

gat gac tta agc ttg acc agc aag ctt caa att gaa gtg gtc att ttc       1056
Asp Asp Leu Ser Leu Thr Ser Lys Leu Gln Ile Glu Val Val Ile Phe
            340                 345                 350

cct aaa aaa atg gac ccg gat gaa tat att aga gaa aat gga cca gaa       1104
Pro Lys Lys Met Asp Pro Asp Glu Tyr Ile Arg Glu Asn Gly Pro Glu
            355                 360                 365

gcc ttt caa aat ctc atc caa cat ggt agg atg act gtc tac caa ttc       1152
```

```
Ala Phe Gln Asn Leu Ile Gln His Gly Arg Met Thr Val Tyr Gln Phe
    370             375             380
```

```
tta aaa gaa tac ttt aaa aaa tcc tac aat cta gat aac gac tcg gac      1200
Leu Lys Glu Tyr Phe Lys Lys Ser Tyr Asn Leu Asp Asn Asp Ser Asp
385             390             395             400
```

```
cgg ttg aaa ttt atc caa acc atg acc aat aaa att ggc aag cta gct      1248
Arg Leu Lys Phe Ile Gln Thr Met Thr Asn Lys Ile Gly Lys Leu Ala
            405             410             415
```

```
tcc ccc ttg gaa agg gaa gtc tat gcc aag gat ttg gca gaa gaa ttt      1296
Ser Pro Leu Glu Arg Glu Val Tyr Ala Lys Asp Leu Ala Glu Glu Phe
            420             425             430
```

```
aac ctg tct tat gat acg att ata agc caa gtt caa agt gaa gcc act      1344
Asn Leu Ser Tyr Asp Thr Ile Ile Ser Gln Val Gln Ser Glu Ala Thr
            435             440             445
```

```
cta aac cag caa gag gct ttg aaa aag gac cgg cat aag gaa ttt tct      1392
Leu Asn Gln Gln Glu Ala Leu Lys Lys Asp Arg His Lys Glu Phe Ser
    450             455             460
```

```
caa gca aga gtg gaa gtc aaa gcc cca agt agt caa aag act aag att      1440
Gln Ala Arg Val Glu Val Lys Ala Pro Ser Ser Gln Lys Thr Lys Ile
465             470             475             480
```

```
gac cgg gcc cag gaa aaa ctt tta aac cga ctc ttt tac tat ccc caa      1488
Asp Arg Ala Gln Glu Lys Leu Leu Asn Arg Leu Phe Tyr Tyr Pro Gln
            485             490             495
```

```
gtt caa gag atc atc gat gct tat aat ccg gac ttt gaa ttt aaa acg      1536
Val Gln Glu Ile Ile Asp Ala Tyr Asn Pro Asp Phe Glu Phe Lys Thr
            500             505             510
```

```
gaa gtc cac cag cgg att tac ctc ttg ttt tta gaa tac agc cag gaa      1584
Glu Val His Gln Arg Ile Tyr Leu Leu Phe Leu Glu Tyr Ser Gln Glu
            515             520             525
```

```
aat gat agc att gat tct ttc atc gat ttt gtc aaa gac aag gag acg      1632
Asn Asp Ser Ile Asp Ser Phe Ile Asp Phe Val Lys Asp Lys Glu Thr
    530             535             540
```

```
aaa gag gtc ata tct gat ata atg tgg aca tcc att gag gtc gaa ccc      1680
Lys Glu Val Ile Ser Asp Ile Met Trp Thr Ser Ile Glu Val Glu Pro
545             550             555             560
```

```
tca gat gaa gaa atc cta gac tac ttg gac tac att gac caa acc tac      1728
Ser Asp Glu Glu Ile Leu Asp Tyr Leu Asp Tyr Ile Asp Gln Thr Tyr
            565             570             575
```

```
ccc ctg gag caa aaa cgc caa gac tgc ttg gag gaa gtc aaa gca gct      1776
Pro Leu Glu Gln Lys Arg Gln Asp Cys Leu Glu Glu Val Lys Ala Ala
            580             585             590
```

```
aaa cag tcc ggt aat aag aag cga gag ctg gaa tta acc aat caa tta      1824
Lys Gln Ser Gly Asn Lys Lys Arg Glu Leu Glu Leu Thr Asn Gln Leu
```

```
            595                   600                   605
att gaa ata aac cgt atg cta aaa caa taa                          1854
Ile Glu Ile Asn Arg Met Leu Lys Gln
    610                   615
```

<210> 64
<211> 617
<212> PRT
<213> Alloiococcus otitidis

<400> 64

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Met Val Arg Ile Pro Glu Glu Thr Ile Asn Gln Ile Arg Ser Gln Ala
1               5                   10                  15


Asp Ile Val Asp Val Ile Gly Gln Tyr Leu Asp Leu Asn Lys Ser Gly
            20                  25                  30


Ala Asn Tyr Phe Ala His Cys Pro Phe His Glu Asp Ser Thr Pro Ser
        35                  40                  45


Phe Ser Val Asn Arg Asp Lys Gln Ile Tyr Lys Cys Phe Ser Cys Lys
    50                  55                  60


Arg Gly Gly Ser Val Phe Ser Phe Ile Gln Glu Lys Glu Gly Leu Ser
65                  70                  75                  80


Phe Pro Glu Ser Val Leu Lys Val Ala Asp Leu Ala Asn Val Asp Leu
            85                  90                  95


Asp Pro Ala Leu Lys Glu Ala Val Gln Gly Gln Pro Asp Lys Ala Asp
            100                 105                 110


Ser Pro Tyr Arg Asp Leu Tyr Thr Ile His Asp Gln Ala Lys Asp Tyr
        115                 120                 125


Tyr Gln Tyr Ile Leu Leu Lys Ala Gln Val Gly Glu Val Ala Tyr Asp
    130                 135                 140


Tyr Leu Gln Asn Arg Gly Ile Ser Arg Glu Val Met Glu Glu Phe Glu
145                 150                 155                 160


Leu Gly Tyr Ser Pro Ser Gln Arg Glu Ser Leu His Leu Tyr Leu Gln
                165                 170                 175
```

Ser Gln Asp Gln Ala Asp Leu Thr Asp Asp Leu Leu Glu Glu Thr Gly
        180   185   190

Leu Phe Ser Lys Arg Glu Val Glu Ser Asp Ser Phe Lys Asp Arg Phe
        195   200   205

Ala Lys Arg Ile Ile Phe Pro Leu Lys Asn Leu Gln Gly Gln Thr Val
    210   215   220

Gly Phe Ser Gly Arg Tyr Phe Gln Asp Glu Pro Asn Gln Asp Phe His
225   230   235   240

His Ala Lys Tyr Leu Asn Ser Pro Glu Thr Lys Ile Phe Asn Lys Arg
            245   250   255

Arg Thr Leu Phe Asn Tyr His Gln Ala Lys Ala Tyr Ile Arg Arg Ala
        260   265   270

Lys Glu Val Val Leu Phe Glu Gly Tyr Met Asp Val Ile Ala Ala Trp
        275   280   285

Gln Ala Gly Val Lys Asn Gly Leu Ala Ser Met Gly Thr Ser Ile Thr
    290   295   300

Ala Asp Gln Val Gln Thr Met Gln Arg Ile Ala Asp Thr Leu Val Leu
305   310   315   320

Ala Phe Asp Gly Asp Glu Ala Gly Leu Glu Ser Ser Lys Lys Ile Leu
            325   330   335

Asp Asp Leu Ser Leu Thr Ser Lys Leu Gln Ile Glu Val Val Ile Phe
        340   345   350

Pro Lys Lys Met Asp Pro Asp Glu Tyr Ile Arg Glu Asn Gly Pro Glu
        355   360   365

Ala Phe Gln Asn Leu Ile Gln His Gly Arg Met Thr Val Tyr Gln Phe
    370   375   380

Leu Lys Glu Tyr Phe Lys Lys Ser Tyr Asn Leu Asp Asn Asp Ser Asp
385   390   395   400

Arg Leu Lys Phe Ile Gln Thr Met Thr Asn Lys Ile Gly Lys Leu Ala

                    405   410   415

Ser Pro Leu Glu Arg Glu Val Tyr Ala Lys Asp Leu Ala Glu Glu Phe
            420   425   430

Asn Leu Ser Tyr Asp Thr Ile Ile Ser Gln Val Gln Ser Glu Ala Thr
            435   440   445

Leu Asn Gln Gln Glu Ala Leu Lys Lys Asp Arg His Lys Glu Phe Ser
    450   455   460

Gln Ala Arg Val Glu Val Lys Ala Pro Ser Ser Gln Lys Thr Lys Ile
465   470   475   480

Asp Arg Ala Gln Glu Lys Leu Leu Asn Arg Leu Phe Tyr Tyr Pro Gln
            485   490   495

Val Gln Glu Ile Ile Asp Ala Tyr Asn Pro Asp Phe Glu Phe Lys Thr
            500   505   510

Glu Val His Gln Arg Ile Tyr Leu Leu Phe Leu Glu Tyr Ser Gln Glu
            515   520   525

Asn Asp Ser Ile Asp Ser Phe Ile Asp Phe Val Lys Asp Lys Glu Thr
    530   535   540

Lys Glu Val Ile Ser Asp Ile Met Trp Thr Ser Ile Glu Val Glu Pro
545   550   555   560

Ser Asp Glu Glu Ile Leu Asp Tyr Leu Asp Tyr Ile Asp Gln Thr Tyr
            565   570   575

Pro Leu Glu Gln Lys Arg Gln Asp Cys Leu Glu Glu Val Lys Ala Ala
            580   585   590

Lys Gln Ser Gly Asn Lys Lys Arg Glu Leu Glu Leu Thr Asn Gln Leu
            595   600   605

Ile Glu Ile Asn Arg Met Leu Lys Gln
    610   615

<210> 65
<211> 987

<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (55)..(987)
<223>

<400> 65
gccagacaat cggacaacta ttaccggaca actttaagcc aggggacatg gaat atg   57
                                                             Met
                                                             1

gaa aac aat gaa aac aat gaa aac aaa gat agc aaa aca ttt aaa tca   105
Glu Asn Asn Glu Asn Asn Glu Asn Lys Asp Ser Lys Thr Phe Lys Ser
              5   10   15

ggt ttt gtc acc ctt ctt ggc cgg ccc aat gtg ggc aag tca acc ctg   153
Gly Phe Val Thr Leu Leu Gly Arg Pro Asn Val Gly Lys Ser Thr Leu
        20   25   30

ctc aac caa ata tta ggc cag aag att acc att atc agt gac aaa ccc   201
Leu Asn Gln Ile Leu Gly Gln Lys Ile Thr Ile Ile Ser Asp Lys Pro
        35   40   45

caa aca acc cgg aat aaa atc cag ggt att tac acc gac caa gcg ggg   249
Gln Thr Thr Arg Asn Lys Ile Gln Gly Ile Tyr Thr Asp Gln Ala Gly
50   55   60   65

caa att gtc ttt atc gac aca cct ggt ata cat aaa ccc aag cac cgc   297
Gln Ile Val Phe Ile Asp Thr Pro Gly Ile His Lys Pro Lys His Arg
                70   75   80

ctg ggc cgg ttt atg gtg gat tcg gct atg tcg acc atc aat gag gtg   345
Leu Gly Arg Phe Met Val Asp Ser Ala Met Ser Thr Ile Asn Glu Val
                85   90   95

gac ctg gtc tta ttt gtg gtc aat gtc agg gaa aag att ggc ccg ggg   393
Asp Leu Val Leu Phe Val Val Asn Val Arg Glu Lys Ile Gly Pro Gly
        100   105   110

gac cgg ttc att atc gac aag ttg cga acc atc gat acg cca gtt ttt   441
Asp Arg Phe Ile Ile Asp Lys Leu Arg Thr Ile Asp Thr Pro Val Phe
        115   120   125

tta att att aac cag att gac cag gtc gat cca aca gac ctc cta ccg   489
Leu Ile Ile Asn Gln Ile Asp Gln Val Asp Pro Thr Asp Leu Leu Pro
130   135   140   145

gtt att agc gac tac caa gag gaa ttc gac ttt gcc gaa gtg gtt cca   537
Val Ile Ser Asp Tyr Gln Glu Glu Phe Asp Phe Ala Glu Val Val Pro
                150   155   160

act tca ggc ttg gaa ggg gaa aat atc cag gag ctc att caa acc atc   585
Thr Ser Gly Leu Glu Gly Glu Asn Ile Gln Glu Leu Ile Gln Thr Ile
                165   170   175

```
aag tct tac cta cct gtt gga ccc caa ttt tac ccg gac gac cag gtc          633
Lys Ser Tyr Leu Pro Val Gly Pro Gln Phe Tyr Pro Asp Asp Gln Val
        180                     185                 190

tcg gac cac ccc gaa tac ttt att att tca gaa ctc atc cgg gag aag          681
Ser Asp His Pro Glu Tyr Phe Ile Ile Ser Glu Leu Ile Arg Glu Lys
        195                     200                 205

gtt tta gac ttg gct aga gaa gag att cct cat tca gta gca gta gta          729
Val Leu Asp Leu Ala Arg Glu Glu Ile Pro His Ser Val Ala Val Val
210                     215                 220                 225

act gag aag gta gac cga aac caa gat ggt aaa gtc caa acc tat gcc          777
Thr Glu Lys Val Asp Arg Asn Gln Asp Gly Lys Val Gln Thr Tyr Ala
                230                 235                 240

acc att att gtc gaa cgc aag agc caa aag ggg att att atc ggc aag          825
Thr Ile Ile Val Glu Arg Lys Ser Gln Lys Gly Ile Ile Ile Gly Lys
                245                 250                 255

caa ggg tcc atg att aaa aaa att ggt agc cta gct cgg cga gat att          873
Gln Gly Ser Met Ile Lys Lys Ile Gly Ser Leu Ala Arg Arg Asp Ile
        260                     265                 270

gag aaa cta ctg gga gat aag att tac ttg gaa ctc tgg gtt aaa gtc          921
Glu Lys Leu Leu Gly Asp Lys Ile Tyr Leu Glu Leu Trp Val Lys Val
        275                     280                 285

caa aga gac tgg cgg gac aag ccc agt cgc tta gaa gac ttt ggc tac          969
Gln Arg Asp Trp Arg Asp Lys Pro Ser Arg Leu Glu Asp Phe Gly Tyr
290                     295                 300                 305

aat gaa gac aac tat tag                                                  987
Asn Glu Asp Asn Tyr
                310
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<210> 66
<211> 310
<212> PRT
<213> Alloiococcus otitidis

<400> 66
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Met Glu Asn Asn Glu Asn Asn Glu Asn Lys Asp Ser Lys Thr Phe Lys
1               5                   10                  15

Ser Gly Phe Val Thr Leu Leu Gly Arg Pro Asn Val Gly Lys Ser Thr
            20                  25                  30

Leu Leu Asn Gln Ile Leu Gly Gln Lys Ile Thr Ile Ile Ser Asp Lys
        35                  40                  45

Pro Gln Thr Thr Arg Asn Lys Ile Gln Gly Ile Tyr Thr Asp Gln Ala
    50                  55                  60
```

```
Gly Gln Ile Val Phe Ile Asp Thr Pro Gly Ile His Lys Pro Lys His
65                  70              75              80

Arg Leu Gly Arg Phe Met Val Asp Ser Ala Met Ser Thr Ile Asn Glu
                85              90              95

Val Asp Leu Val Leu Phe Val Val Asn Val Arg Glu Lys Ile Gly Pro
            100             105             110

Gly Asp Arg Phe Ile Ile Asp Lys Leu Arg Thr Ile Asp Thr Pro Val
        115             120             125

Phe Leu Ile Ile Asn Gln Ile Asp Gln Val Asp Pro Thr Asp Leu Leu
        130             135             140

Pro Val Ile Ser Asp Tyr Gln Glu Glu Phe Asp Phe Ala Glu Val Val
145             150             155             160

Pro Thr Ser Gly Leu Glu Gly Glu Asn Ile Gln Glu Leu Ile Gln Thr
                165             170             175

Ile Lys Ser Tyr Leu Pro Val Gly Pro Gln Phe Tyr Pro Asp Asp Gln
            180             185             190

Val Ser Asp His Pro Glu Tyr Phe Ile Ile Ser Glu Leu Ile Arg Glu
        195             200             205

Lys Val Leu Asp Leu Ala Arg Glu Glu Ile Pro His Ser Val Ala Val
210             215             220

Val Thr Glu Lys Val Asp Arg Asn Gln Asp Gly Lys Val Gln Thr Tyr
225             230             235             240

Ala Thr Ile Ile Val Glu Arg Lys Ser Gln Lys Gly Ile Ile Ile Gly
                245             250             255

Lys Gln Gly Ser Met Ile Lys Lys Ile Gly Ser Leu Ala Arg Arg Asp
            260             265             270

Ile Glu Lys Leu Leu Gly Asp Lys Ile Tyr Leu Glu Leu Trp Val Lys
        275             280             285
```

```
Val Gln Arg Asp Trp Arg Asp Lys Pro Ser Arg Leu Glu Asp Phe Gly
    290                 295             300

Tyr Asn Glu Asp Asn Tyr
305             310


<210> 67
<211> 1557
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (46)..(1557)
<223>

<400> 67
catgtctatg ttactttaat cagtggaaaa caagaggaga tcatt gtg att tcc tct      57
                                                    Met Ile Ser Ser
                                                    1

ttc tat tta gta gga gtc ttg aga ttg agt agt gaa aat aaa tta acc      105
Phe Tyr Leu Val Gly Val Leu Arg Leu Ser Ser Glu Asn Lys Leu Thr
5               10              15              20

ttc aaa cac ttc ctt gca aac cag ttg acc aaa cga gac aat tta caa      153
Phe Lys His Phe Leu Ala Asn Gln Leu Thr Lys Arg Asp Asn Leu Gln
            25              30              35

atc ccc cgt tgg caa att ttt gcc gtt tta ttt aca gga gcc gtg att      201
Ile Pro Arg Trp Gln Ile Phe Ala Val Leu Phe Thr Gly Ala Val Ile
            40              45              50

gtg gtt ctc aac caa acg gcc atg tct acc gcc ttg cct aat atg att      249
Val Val Leu Asn Gln Thr Ala Met Ser Thr Ala Leu Pro Asn Met Ile
        55              60              65

gaa agt ttg ggc att gac cct agc cta ggc cag tgg att gtc tcg ggt      297
Glu Ser Leu Gly Ile Asp Pro Ser Leu Gly Gln Trp Ile Val Ser Gly
70              75              80

tat acc ttg gtc aaa ggg att atg gtc ccc ata acc gcc ttt gcc atg      345
Tyr Thr Leu Val Lys Gly Ile Met Val Pro Ile Thr Ala Phe Ala Met
85              90              95              100

acc aag tac cgg aca cgg aac ttt ttt att tta atg ttg gcc ctc ttc      393
Thr Lys Tyr Arg Thr Arg Asn Phe Phe Ile Leu Met Leu Ala Leu Phe
            105             110             115

tgt acc ggt agt ttt ttg act ggt ctg ggc ttt aat ttt ccg gtt gtg      441
Cys Thr Gly Ser Phe Leu Thr Gly Leu Gly Phe Asn Phe Pro Val Val
            120             125             130

gtc atg ggg aca gtc atc cag ggt ata gcg gct ggg atg atc atc ccc      489
```

```
Val Met Gly Thr Val Ile Gln Gly Ile Ala Ala Gly Met Ile Ile Pro
    135             140             145

ttg atg cag acc gtc ctc ttg acc ttg atg ccg gtt gaa agc cga ggc      537
Leu Met Gln Thr Val Leu Leu Thr Leu Met Pro Val Glu Ser Arg Gly
    150             155             160

act gct atg ggg gta atg agt ggg gtt att ggt att ggt cca gca ctg      585
Thr Ala Met Gly Val Met Ser Gly Val Ile Gly Ile Gly Pro Ala Leu
165             170             175             180

ggt ccc ctt gtc ggt ggg gtc att gtt gat gct ttc acc tgg gaa att      633
Gly Pro Leu Val Gly Gly Val Ile Val Asp Ala Phe Thr Trp Glu Ile
                185             190             195

tta ttc tac atc tgg gcc tta atc acc ctt tta ttg gtt cct tta act      681
Leu Phe Tyr Ile Trp Ala Leu Ile Thr Leu Leu Leu Val Pro Leu Thr
            200             205             210

tgg ctg gtc tta ccc gat gta ttg cca aat gca gat tta acc att aat      729
Trp Leu Val Leu Pro Asp Val Leu Pro Asn Ala Asp Leu Thr Ile Asn
        215             220             225

tgg gcc aat atc cgg gac tcc ctc att ggt ttt ggc ctc ctc ctc ttt      777
Trp Ala Asn Ile Arg Asp Ser Leu Ile Gly Phe Gly Leu Leu Leu Phe
    230             235             240

agc ttg tca gtc ttt ggt tct tcc ggt ttt tct tcg gtc att gcc tgg      825
Ser Leu Ser Val Phe Gly Ser Ser Gly Phe Ser Ser Val Ile Ala Trp
245             250             255             260

gtc agc ttg ctt atc ggt tta gtc ttt gtc gcc aag ttt atc cac ttc      873
Val Ser Leu Leu Ile Gly Leu Val Phe Val Ala Lys Phe Ile His Phe
                265             270             275

aac ctc aag gca gac caa cca atc tta aat ctt aga ctc ttt aaa aaa      921
Asn Leu Lys Ala Asp Gln Pro Ile Leu Asn Leu Arg Leu Phe Lys Lys
            280             285             290

acc tat tac cgt cgg gct gtc ttg gta gcc acc ttg ggg att gtc att      969
Thr Tyr Tyr Arg Arg Ala Val Leu Val Ala Thr Leu Gly Ile Val Ile
        295             300             305

att tct tgt cta tcc aac att atc cct att tat gtt caa act gtt agg     1017
Ile Ser Cys Leu Ser Asn Ile Ile Pro Ile Tyr Val Gln Thr Val Arg
    310             315             320

ggc ttg ggg gct tcc ata gca ggc tta atc tta atg cca gct ggt atc     1065
Gly Leu Gly Ala Ser Ile Ala Gly Leu Ile Leu Met Pro Ala Gly Ile
325             330             335             340

atc aaa acc atc tta gct cct atc tca ggc aaa ctt tat gac aag gtt     1113
Ile Lys Thr Ile Leu Ala Pro Ile Ser Gly Lys Leu Tyr Asp Lys Val
                345             350             355

gga gtg gct cgg att ggc ctt atc ggt ggt atc tta ctt tta gtt ggg     1161
Gly Val Ala Arg Ile Gly Leu Ile Gly Gly Ile Leu Leu Leu Val Gly
```

```
            360                   365                   370

tcc tta tta cta gtt acc ctc aat gaa gct agc tcc ctt tac tta ctg      1209
Ser Leu Leu Leu Val Thr Leu Asn Glu Ala Ser Ser Leu Tyr Leu Leu
        375                   380                   385

atg att tac tac ggc atc tta tca gcc ggt ttt ggc ttg ttt aat atc      1257
Met Ile Tyr Tyr Gly Ile Leu Ser Ala Gly Phe Gly Leu Phe Asn Ile
        390                   395                   400

cct att acc act gct ggc atg aat att atg gcc aag gaa gat atg gga      1305
Pro Ile Thr Thr Ala Gly Met Asn Ile Met Ala Lys Glu Asp Met Gly
405                   410                   415                   420

cat gcg act tca gcc cgg caa acg gtc cgg caa atc tct tca agt ttt      1353
His Ala Thr Ser Ala Arg Gln Thr Val Arg Gln Ile Ser Ser Ser Phe
                425                   430                   435

gcc gtt tcc ctc tcc ttt atc atc atg acc ctg gtg act att gcc act      1401
Ala Val Ser Leu Ser Phe Ile Ile Met Thr Leu Val Thr Ile Ala Thr
                440                   445                   450

tcc ggc caa tcg gtg ggg gtt ttc caa gat ggc ggt ccg aca gac tta      1449
Ser Gly Gln Ser Val Gly Val Phe Gln Asp Gly Gly Pro Thr Asp Leu
            455                   460                   465

aat atg gca gga gtc cga ggc gcc ttt atc ttg gtg gct ata ttt tca      1497
Asn Met Ala Gly Val Arg Gly Ala Phe Ile Leu Val Ala Ile Phe Ser
        470                   475                   480

atc cta gcc atg atc ttg atc ttc ttt tta aaa gac cct aaa gaa aaa      1545
Ile Leu Ala Met Ile Leu Ile Phe Phe Leu Lys Asp Pro Lys Glu Lys
485                   490                   495                   500

cca gac caa tag                                                       1557
Pro Asp Gln
```

```
<210> 68
<211> 503
<212> PRT
<213> Alloiococcus otitidis

<400> 68
Met Ile Ser Ser Phe Tyr Leu Val Gly Val Leu Arg Leu Ser Ser Glu
1               5                   10                  15


Asn Lys Leu Thr Phe Lys His Phe Leu Ala Asn Gln Leu Thr Lys Arg
            20                  25                  30


Asp Asn Leu Gln Ile Pro Arg Trp Gln Ile Phe Ala Val Leu Phe Thr
        35                  40                  45


Gly Ala Val Ile Val Val Leu Asn Gln Thr Ala Met Ser Thr Ala Leu
```

                    50   55   60

Pro Asn Met Ile Glu Ser Leu Gly Ile Asp Pro Ser Leu Gly Gln Trp
65   70   75   80

Ile Val Ser Gly Tyr Thr Leu Val Lys Gly Ile Met Val Pro Ile Thr
                85   90   95

Ala Phe Ala Met Thr Lys Tyr Arg Thr Arg Asn Phe Phe Ile Leu Met
            100   105   110

Leu Ala Leu Phe Cys Thr Gly Ser Phe Leu Thr Gly Leu Gly Phe Asn
            115   120   125

Phe Pro Val Val Val Met Gly Thr Val Ile Gln Gly Ile Ala Ala Gly
        130   135   140

Met Ile Ile Pro Leu Met Gln Thr Val Leu Leu Thr Leu Met Pro Val
145   150   155   160

Glu Ser Arg Gly Thr Ala Met Gly Val Met Ser Gly Val Ile Gly Ile
                165   170   175

Gly Pro Ala Leu Gly Pro Leu Val Gly Gly Val Ile Val Asp Ala Phe
            180   185   190

Thr Trp Glu Ile Leu Phe Tyr Ile Trp Ala Leu Ile Thr Leu Leu Leu
        195   200   205

Val Pro Leu Thr Trp Leu Val Leu Pro Asp Val Leu Pro Asn Ala Asp
    210   215   220

Leu Thr Ile Asn Trp Ala Asn Ile Arg Asp Ser Leu Ile Gly Phe Gly
225   230   235   240

Leu Leu Leu Phe Ser Leu Ser Val Phe Gly Ser Ser Gly Phe Ser Ser
            245   250   255

Val Ile Ala Trp Val Ser Leu Leu Ile Gly Leu Val Phe Val Ala Lys
        260   265   270

Phe Ile His Phe Asn Leu Lys Ala Asp Gln Pro Ile Leu Asn Leu Arg
    275   280   285

```
Leu Phe Lys Lys Thr Tyr Tyr Arg Arg Ala Val Leu Val Ala Thr Leu
    290             295             300
```

```
Gly Ile Val Ile Ile Ser Cys Leu Ser Asn Ile Ile Pro Ile Tyr Val
305             310             315             320
```

```
Gln Thr Val Arg Gly Leu Gly Ala Ser Ile Ala Gly Leu Ile Leu Met
            325             330             335
```

```
Pro Ala Gly Ile Ile Lys Thr Ile Leu Ala Pro Ile Ser Gly Lys Leu
            340             345             350
```

```
Tyr Asp Lys Val Gly Val Ala Arg Ile Gly Leu Ile Gly Gly Ile Leu
        355             360             365
```

```
Leu Leu Val Gly Ser Leu Leu Leu Val Thr Leu Asn Glu Ala Ser Ser
    370             375             380
```

```
Leu Tyr Leu Leu Met Ile Tyr Tyr Gly Ile Leu Ser Ala Gly Phe Gly
385             390             395             400
```

```
Leu Phe Asn Ile Pro Ile Thr Thr Ala Gly Met Asn Ile Met Ala Lys
            405             410             415
```

```
Glu Asp Met Gly His Ala Thr Ser Ala Arg Gln Thr Val Arg Gln Ile
            420             425             430
```

```
Ser Ser Ser Phe Ala Val Ser Leu Ser Phe Ile Ile Met Thr Leu Val
        435             440             445
```

```
Thr Ile Ala Thr Ser Gly Gln Ser Val Gly Val Phe Gln Asp Gly Gly
    450             455             460
```

```
Pro Thr Asp Leu Asn Met Ala Gly Val Arg Gly Ala Phe Ile Leu Val
465             470             475             480
```

```
Ala Ile Phe Ser Ile Leu Ala Met Ile Leu Ile Phe Phe Leu Lys Asp
            485             490             495
```

```
Pro Lys Glu Lys Pro Asp Gln
            500
```

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<210> 69
<211> 4392
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (58)..(4392)
<223>

<400> 69
aagggttcag gactttcgta tctggccctt tttggctcat tagaaagcag ggcaaag          57
```

```
atg tca ctc aat caa aaa gaa atg tat caa gta ttg ·atg cag caa gtc          105
Met Ser Leu Asn Gln Lys Glu Met Tyr Gln Val Leu Met Gln Gln Val
1               5               10              15

cac tta gaa gaa cac cta caa gac cga ccc ctt ctt aaa gcc ggc agt          153
His Leu Glu Glu His Leu Gln Asp Arg Pro Leu Leu Lys Ala Gly Ser
            20              25              30

ttg aag caa att gtt gtt tac aag gct caa caa gcc tgg gac ctg acc          201
Leu Lys Gln Ile Val Val Tyr Lys Ala Gln Gln Ala Trp Asp Leu Thr
        35              40              45

ctc caa ttt cct cag atc ctc cct ttt aag gac ttc caa gtt ttg gag          249
Leu Gln Phe Pro Gln Ile Leu Pro Phe Lys Asp Phe Gln Val Leu Glu
    50              55              60

tct gcc ctc ttg cag cat atc cca gaa gtc aac cag atc cat tta agg          297
Ser Ala Leu Leu Gln His Ile Pro Glu Val Asn Gln Ile His Leu Arg
65              70              75              80

gtt gat gcc caa gat gac agt ttt gac cag gac ctc ctc cag gac tat          345
Val Asp Ala Gln Asp Asp Ser Phe Asp Gln Asp Leu Leu Gln Asp Tyr
            85              90              95

tgg cct aag gcg gtg aag ttt agc gga gtc gat tct ccc ctt tgc aat          393
Trp Pro Lys Ala Val Lys Phe Ser Gly Val Asp Ser Pro Leu Cys Asn
            100             105             110

gac tta cta gac aag acc ctc cct tat cta gat ggg aag caa gtt tac          441
Asp Leu Leu Asp Lys Thr Leu Pro Tyr Leu Asp Gly Lys Gln Val Tyr
        115             120             125

ttt gac ctg gac cat gaa gtg acc cgg gac aag ttt gac cat gac ttc          489
Phe Asp Leu Asp His Glu Val Thr Arg Asp Lys Phe Asp His Asp Phe
    130             135             140

cta cct cgg atc caa gct ggc tac cag caa gtg ggc ttt ccc aac cac          537
Leu Pro Arg Ile Gln Ala Gly Tyr Gln Gln Val Gly Phe Pro Asn His
145             150             155             160

ttt aaa atc aag gct agg gtc gat gcc cag aaa aat tca gat caa att          585
```

```
Phe Lys Ile Lys Ala Arg Val Asp Ala Gln Lys Asn Ser Asp Gln Ile
             165             170             175
```

```
gcc gcc ttc cgt aaa gaa aaa gaa gaa aaa gac cag gcc ttg tct caa    633
Ala Ala Phe Arg Lys Glu Lys Glu Glu Lys Asp Gln Ala Leu Ser Gln
             180             185             190
```

```
gag cta acc aac caa ttt atc aag gcc agc caa aag aaa gaa gaa ggg    681
Glu Leu Thr Asn Gln Phe Ile Lys Ala Ser Gln Lys Lys Glu Glu Gly
             195             200             205
```

```
gga tcc aaa gcc aag tcg gag gcc ttg aag atg ggc cgg gcc atc cct    729
Gly Ser Lys Ala Lys Ser Glu Ala Leu Lys Met Gly Arg Ala Ile Pro
         210             215             220
```

```
gac cac gaa acg att acc cag atg gtt gat gtg gaa gaa gaa gag agc    777
Asp His Glu Thr Ile Thr Gln Met Val Asp Val Glu Glu Glu Glu Ser
225             230             235             240
```

```
cgt ctg acc ttt gaa gga tac gtt ttt gat gtg gaa atc aaa tcc ctc    825
Arg Leu Thr Phe Glu Gly Tyr Val Phe Asp Val Glu Ile Lys Ser Leu
             245             250             255
```

```
cgg tca gat aga aag ctc ctt ctc ttt aaa atg acc gac tat agc tct    873
Arg Ser Asp Arg Lys Leu Leu Leu Phe Lys Met Thr Asp Tyr Ser Ser
             260             265             270
```

```
tcc ttc cta ttc aaa aaa ttc tct aat aat tct tct gac gaa gcc cta    921
Ser Phe Leu Phe Lys Lys Phe Ser Asn Asn Ser Ser Asp Glu Ala Leu
             275             280             285
```

```
ttt gac caa gtc caa gag gga atg tgg ctc aag gtt aga ggc agt gtt    969
Phe Asp Gln Val Gln Glu Gly Met Trp Leu Lys Val Arg Gly Ser Val
         290             295             300
```

```
caa gaa gat acc ttt gtc aaa gac cta gtt gtc atg gcc caa gac atc    1017
Gln Glu Asp Thr Phe Val Lys Asp Leu Val Val Met Ala Gln Asp Ile
305             310             315             320
```

```
caa gag gtc aaa aaa gaa ccc cgg cgg gac ctg gct aag gaa ggg gag    1065
Gln Glu Val Lys Lys Glu Pro Arg Arg Asp Leu Ala Lys Glu Gly Glu
             325             330             335
```

```
aag agg gtg gaa ctt cat gcc cat acc acc atg agt cag atg gac ggt    1113
Lys Arg Val Glu Leu His Ala His Thr Thr Met Ser Gln Met Asp Gly
             340             345             350
```

```
ttg gtg ccg gcc aag gat ttg gtc aag caa gca gcc gct ttt gac caa    1161
Leu Val Pro Ala Lys Asp Leu Val Lys Gln Ala Ala Ala Phe Asp Gln
             355             360             365
```

```
ccg gct att gcc atc act gat cat gct gta gtc caa tcc ttc cca gag    1209
Pro Ala Ile Ala Ile Thr Asp His Ala Val Val Gln Ser Phe Pro Glu
370             375             380
```

```
gcc cat tat gct ggc tta gac act ggt gtt aaa att ctt tac ggt gtg    1257
Ala His Tyr Ala Gly Leu Asp Thr Gly Val Lys Ile Leu Tyr Gly Val
```

```
385                    390                    395                    400

gaa gcc aat ttg gtt agt gat ggc gaa ttg gta gca tac aat ccg gcc    1305
Glu Ala Asn Leu Val Ser Asp Gly Glu Leu Val Ala Tyr Asn Pro Ala
                405                    410                    415

gat ata aag ctg gaa gag gca act tat gtg gtc ttc gac gtg gaa aca    1353
Asp Ile Lys Leu Glu Glu Ala Thr Tyr Val Val Phe Asp Val Glu Thr
                420                    425                    430

acc gga cta tcg gct cgt tat gac caa atc att gaa ttg gcc gct gtg    1401
Thr Gly Leu Ser Ala Arg Tyr Asp Gln Ile Ile Glu Leu Ala Ala Val
                435                    440                    445

aag atg gaa aat ggg gaa atc gtt tct gaa ttc caa gaa ttt att gac    1449
Lys Met Glu Asn Gly Glu Ile Val Ser Glu Phe Gln Glu Phe Ile Asp
        450                    455                    460

cca ggc cag ccc ttg tct gag act acg acc aat ttg acc ggg atc acc    1497
Pro Gly Gln Pro Leu Ser Glu Thr Thr Thr Asn Leu Thr Gly Ile Thr
465                    470                    475                    480

gat gac atg gtc caa gga tcc aaa agt gaa gac gaa gtc ctc cat gcc    1545
Asp Asp Met Val Gln Gly Ser Lys Ser Glu Asp Glu Val Leu His Ala
                485                    490                    495

ttt caa gcc ttt tca gaa ggc act gtc ttg gtc gcc cat aac gct tcc    1593
Phe Gln Ala Phe Ser Glu Gly Thr Val Leu Val Ala His Asn Ala Ser
            500                    505                    510

ttt gac atg ggc ttt atc aat acg gcc tac caa cga cat ggc cta gga    1641
Phe Asp Met Gly Phe Ile Asn Thr Ala Tyr Gln Arg His Gly Leu Gly
        515                    520                    525

caa gct gac cag cct gtg att gat acc ttg gaa ttg tcc cgc atg ctc    1689
Gln Ala Asp Gln Pro Val Ile Asp Thr Leu Glu Leu Ser Arg Met Leu
        530                    535                    540

cac cca aac ttg aaa agc cac cgg tta aac act ctg gct aag cgg tat    1737
His Pro Asn Leu Lys Ser His Arg Leu Asn Thr Leu Ala Lys Arg Tyr
545                    550                    555                    560

gac gtg gcc tta gaa cac cac cac cgg gcc atc tat gac tcg gag tca    1785
Asp Val Ala Leu Glu His His His Arg Ala Ile Tyr Asp Ser Glu Ser
                565                    570                    575

acg gct aaa ctc ttg tgg atc ttc tta aaa gaa gcc aaa gac caa tat    1833
Thr Ala Lys Leu Leu Trp Ile Phe Leu Lys Glu Ala Lys Asp Gln Tyr
            580                    585                    590

gac atg act agc cac caa gac ttg aat agc cag gtg ggg gaa ggc gag    1881
Asp Met Thr Ser His Gln Asp Leu Asn Ser Gln Val Gly Glu Gly Glu
        595                    600                    605

gct tac aag cag gcc cgg cca acc cat gcc agt att ttg gtc aag aat    1929
Ala Tyr Lys Gln Ala Arg Pro Thr His Ala Ser Ile Leu Val Lys Asn
        610                    615                    620
```

```
caa aaa ggc ttg aaa aac ctc ttt aaa att gtc tcc cac gcc cat gtc        1977
Gln Lys Gly Leu Lys Asn Leu Phe Lys Ile Val Ser His Ala His Val
625             630             635             640

aac tac ttc tac cgg gtt ccc cgt ata cct aag tct atc ttg agc aag        2025
Asn Tyr Phe Tyr Arg Val Pro Arg Ile Pro Lys Ser Ile Leu Ser Lys
                645             650             655

tac cgg gaa ggc ctt ttg gtt ggg tct ggt tgc gga cag gga gag ctc        2073
Tyr Arg Glu Gly Leu Leu Val Gly Ser Gly Cys Gly Gln Gly Glu Leu
            660             665             670

ttt gag gct att atg caa aag ggc tat gac gaa gcc ttg gca gtt gcc        2121
Phe Glu Ala Ile Met Gln Lys Gly Tyr Asp Glu Ala Leu Ala Val Ala
            675             680             685

cag gac tat gat tat att gaa gtt atg ccc aag tca gcc tat att gac        2169
Gln Asp Tyr Asp Tyr Ile Glu Val Met Pro Lys Ser Ala Tyr Ile Asp
        690             695             700

ctc ttg gac cgg gac tta atc aag gat gag gca acc ctt gaa gaa atg        2217
Leu Leu Asp Arg Asp Leu Ile Lys Asp Glu Ala Thr Leu Glu Glu Met
705             710             715             720

att gaa aac ctg gtt aaa ata ggc cat gaa ctt gat ata ccc gtg gta        2265
Ile Glu Asn Leu Val Lys Ile Gly His Glu Leu Asp Ile Pro Val Val
                725             730             735

gct aca ggg aat gtc cac tac cta aac cca gaa gat gcc gtt tta cgg        2313
Ala Thr Gly Asn Val His Tyr Leu Asn Pro Glu Asp Ala Val Leu Arg
            740             745             750

gat atc ctc ctg gaa act gcc aaa aag gga gcc ttc tcc aaa gcc cgg        2361
Asp Ile Leu Leu Glu Thr Ala Lys Lys Gly Ala Phe Ser Lys Ala Arg
            755             760             765

aac cca gaa gtc cac ttt aga aca aca gat gaa atg tta gaa gag ttt        2409
Asn Pro Glu Val His Phe Arg Thr Thr Asp Glu Met Leu Glu Glu Phe
        770             775             780

tcc ttc cta ggc cag gac cag gct tat gag att gtg gtc acc aac acc        2457
Ser Phe Leu Gly Gln Asp Gln Ala Tyr Glu Ile Val Val Thr Asn Thr
785             790             795             800

caa aaa att gct gat tct atc gaa tca atc tct cct gtc aag gaa ggc        2505
Gln Lys Ile Ala Asp Ser Ile Glu Ser Ile Ser Pro Val Lys Glu Gly
                805             810             815

ctc tat gcc ccg aaa atg gaa ggg tcg gac caa gag ata cgt cag atg        2553
Leu Tyr Ala Pro Lys Met Glu Gly Ser Asp Gln Glu Ile Arg Gln Met
            820             825             830

agt tac aag caa gcc aag gct ctc tat ggc gac ccc ttg cca agt att        2601
Ser Tyr Lys Gln Ala Lys Ala Leu Tyr Gly Asp Pro Leu Pro Ser Ile
        835             840             845
```

```
gta gag gaa agg ctc gaa aaa gag ttg aag agt att att gac aac aat      2649
Val Glu Glu Arg Leu Glu Lys Glu Leu Lys Ser Ile Ile Asp Asn Asn
    850             855             860

ttc tct gtc att tac tta att tcc cag aaa ttg gtc aaa aaa agt gtt      2697
Phe Ser Val Ile Tyr Leu Ile Ser Gln Lys Leu Val Lys Lys Ser Val
865             870             875             880

gaa gat ggc tat ttg gtt ggt tcc agg ggg tcg gtt ggg tca agc ttt      2745
Glu Asp Gly Tyr Leu Val Gly Ser Arg Gly Ser Val Gly Ser Ser Phe
                885             890             895

gtg gcc acc atg acc ggg atc aca gaa gtc aac cca cta ccg ccc cac      2793
Val Ala Thr Met Thr Gly Ile Thr Glu Val Asn Pro Leu Pro Pro His
            900             905             910

tac cgc tgt cct aac tgc cag cac acc gaa ttc ttc aca aat ggg gaa      2841
Tyr Arg Cys Pro Asn Cys Gln His Thr Glu Phe Phe Thr Asn Gly Glu
        915             920             925

gtg ggg tcc ggc ttt gac tta gag gcc aaa aaa tgt ccg gaa tgt caa      2889
Val Gly Ser Gly Phe Asp Leu Glu Ala Lys Lys Cys Pro Glu Cys Gln
    930             935             940

agc cta atg gaa tca gac ggc cac gac att ccc ttc gaa acc ttc ctt      2937
Ser Leu Met Glu Ser Asp Gly His Asp Ile Pro Phe Glu Thr Phe Leu
945             950             955             960

ggt ttt aat ggg gac aag gtg cca gat atc gat ttg aac ttc tca ggt      2985
Gly Phe Asn Gly Asp Lys Val Pro Asp Ile Asp Leu Asn Phe Ser Gly
                965             970             975

gaa tac cag gcc aag gcc cac aac tat acc aag gtt ttg ttt gga gaa      3033
Glu Tyr Gln Ala Lys Ala His Asn Tyr Thr Lys Val Leu Phe Gly Glu
            980             985             990

gac cat gtc tac cgg gca ggg acc atc acg acg att gct gac aag acg      3081
Asp His Val Tyr Arg Ala Gly Thr Ile Thr Thr Ile Ala Asp Lys Thr
        995             1000            1005

gcc ttt ggt ttt gtc aag ggt tat gaa agg gac aag cag ata aac tac      3129
Ala Phe Gly Phe Val Lys Gly Tyr Glu Arg Asp Lys Gln Ile Asn Tyr
    1010            1015            1020

cgg tcg gct gaa gtg gac cgg ctg tca gat ggt tta acc gga gtg aga      3177
Arg Ser Ala Glu Val Asp Arg Leu Ser Asp Gly Leu Thr Gly Val Arg
1025            1030            1035            1040

cgg tca acc ggc cag cac cca gga ggg att atc gtc ata ccg gat gac      3225
Arg Ser Thr Gly Gln His Pro Gly Gly Ile Ile Val Ile Pro Asp Asp
                1045            1050            1055

atg gat gtg ttt gat ttc acc ccc atc cag tac ccg gct gac gac cag      3273
Met Asp Val Phe Asp Phe Thr Pro Ile Gln Tyr Pro Ala Asp Asp Gln
            1060            1065            1070

acg gct gag tgg caa act acc cac ttt gac ttc cac tcc atc gac gaa      3321
```

Thr Ala Glu Trp Gln Thr Thr His Phe Asp Phe His Ser Ile Asp Glu
        1075   1080   1085

aac gtc ttg aag ctg gat atc ctg gga cat gat gac ccg acc atg atc   3369
Asn Val Leu Lys Leu Asp Ile Leu Gly His Asp Asp Pro Thr Met Ile
        1090   1095   1100

cga aaa ctc cag gac ttg tcc ggc ttt gac cct caa gaa ata ccg gta   3417
Arg Lys Leu Gln Asp Leu Ser Gly Phe Asp Pro Gln Glu Ile Pro Val
1105   1110   1115   1120

agt gat gaa gat gtt atg aaa att ttc tca ggc ccg gaa gtt cta ggg   3465
Ser Asp Glu Asp Val Met Lys Ile Phe Ser Gly Pro Glu Val Leu Gly
                1125   1130   1135

gtg acc cca gag caa att ttc tcc aat acc gga act ctc gga gta cct   3513
Val Thr Pro Glu Gln Ile Phe Ser Asn Thr Gly Thr Leu Gly Val Pro
                1140   1145   1150

gaa ttt ggt acc caa ttt gtc cga gaa atg tta gag caa acc cac ccc   3561
Glu Phe Gly Thr Gln Phe Val Arg Glu Met Leu Glu Gln Thr His Pro
                1155   1160   1165

tct acc ttt gct gaa ctc ttg cag atc tca ggc ctc tcc cac ggg aca   3609
Ser Thr Phe Ala Glu Leu Leu Gln Ile Ser Gly Leu Ser His Gly Thr
        1170   1175   1180

gat gtt tgg ctg ggc aat gct gaa gaa tta att cgc aac cac aac att   3657
Asp Val Trp Leu Gly Asn Ala Glu Glu Leu Ile Arg Asn His Asn Ile
1185   1190   1195   1200

ccc ttg tcc gag gtg atc ggc tgc cgg gat gat atc atg gtc tac ctt   3705
Pro Leu Ser Glu Val Ile Gly Cys Arg Asp Asp Ile Met Val Tyr Leu
                1205   1210   1215

caa cac caa ggt ctt gaa gac agc ctg gcc ttt aag att atg gaa ttt   3753
Gln His Gln Gly Leu Glu Asp Ser Leu Ala Phe Lys Ile Met Glu Phe
                1220   1225   1230

gtt cgt aag ggt cgg ggc ttg caa gat gac tgg att gct acc atg aaa   3801
Val Arg Lys Gly Arg Gly Leu Gln Asp Asp Trp Ile Ala Thr Met Lys
                1235   1240   1245

gaa aat gat gtt cct gat tgg tat att gaa tcc tgc aaa aaa atc aag   3849
Glu Asn Asp Val Pro Asp Trp Tyr Ile Glu Ser Cys Lys Lys Ile Lys
        1250   1255   1260

tac atg ttc cct aaa gcc cac gca gct gcc tat gtc ttg atg gcc ctt   3897
Tyr Met Phe Pro Lys Ala His Ala Ala Ala Tyr Val Leu Met Ala Leu
1265   1270   1275   1280

agg gta gct tac ttt aaa gtc cac tac ccc ctt tac tac tac gct gcc   3945
Arg Val Ala Tyr Phe Lys Val His Tyr Pro Leu Tyr Tyr Tyr Ala Ala
                1285   1290   1295

tac ttt tcc atc cgg gct agt gat ttt gac tta att gct atg gtc aag   3993
Tyr Phe Ser Ile Arg Ala Ser Asp Phe Asp Leu Ile Ala Met Val Lys

```
                1300              1305              1310

ggc aag gaa ggc att aaa ggg gct atg aag gaa atc agg gac aag gaa     4041
Gly Lys Glu Gly Ile Lys Gly Ala Met Lys Glu Ile Arg Asp Lys Glu
        1315              1320              1325

aga gaa aaa act gcc aca gct aag gac aaa gcc ttg ctc acc gtc ctt     4089
Arg Glu Lys Thr Ala Thr Ala Lys Asp Lys Ala Leu Leu Thr Val Leu
        1330              1335              1340

gaa gta gcc aat gaa atg gtt gaa cgg ggt ttt gac ttc aag atg gtg     4137
Glu Val Ala Asn Glu Met Val Glu Arg Gly Phe Asp Phe Lys Met Val
1345              1350              1355              1360

gac atc aac aag tcc caa gcc aaa gac ttt gtc atc gaa gac aat ggc     4185
Asp Ile Asn Lys Ser Gln Ala Lys Asp Phe Val Ile Glu Asp Asn Gly
            1365              1370              1375

ctt cgt gct cca ttt agg gca gtc cct tcc ttg ggg tcc agt gcc gcc     4233
Leu Arg Ala Pro Phe Arg Ala Val Pro Ser Leu Gly Ser Ser Ala Ala
            1380              1385              1390

cag gct gtc att gat gcc agg gag gac agc gac ttc ttg tcc aag gaa     4281
Gln Ala Val Ile Asp Ala Arg Glu Asp Ser Asp Phe Leu Ser Lys Glu
        1395              1400              1405

gac cta tca aaa cgg ggc aag ttg tcg aaa acg gtc atg gac tac ctg     4329
Asp Leu Ser Lys Arg Gly Lys Leu Ser Lys Thr Val Met Asp Tyr Leu
        1410              1415              1420

gac aat aac cac gtt tta gac cac ctg ccg gac gaa aac caa ctt tcc     4377
Asp Asn Asn His Val Leu Asp His Leu Pro Asp Glu Asn Gln Leu Ser
1425              1430              1435              1440

ctc ttt gac ttt taa                                                  4392
Leu Phe Asp Phe


<210> 70
<211> 1444
<212> PRT
<213> Alloiococcus otitidis

<400> 70
Met Ser Leu Asn Gln Lys Glu Met Tyr Gln Val Leu Met Gln Gln Val
1               5               10              15


His Leu Glu Glu His Leu Gln Asp Arg Pro Leu Leu Lys Ala Gly Ser
            20              25              30


Leu Lys Gln Ile Val Val Tyr Lys Ala Gln Gln Ala Trp Asp Leu Thr
        35              40              45


Leu Gln Phe Pro Gln Ile Leu Pro Phe Lys Asp Phe Gln Val Leu Glu
```

```
              50                      55                      60

Ser Ala Leu Leu Gln His Ile Pro Glu Val Asn Gln Ile His Leu Arg
65                  70                  75                  80

Val Asp Ala Gln Asp Asp Ser Phe Asp Gln Asp Leu Leu Gln Asp Tyr
                85                  90                  95

Trp Pro Lys Ala Val Lys Phe Ser Gly Val Asp Ser Pro Leu Cys Asn
            100                 105                 110

Asp Leu Leu Asp Lys Thr Leu Pro Tyr Leu Asp Gly Lys Gln Val Tyr
            115                 120                 125

Phe Asp Leu Asp His Glu Val Thr Arg Asp Lys Phe Asp His Asp Phe
    130                 135                 140

Leu Pro Arg Ile Gln Ala Gly Tyr Gln Gln Val Gly Phe Pro Asn His
145                 150                 155                 160

Phe Lys Ile Lys Ala Arg Val Asp Ala Gln Lys Asn Ser Asp Gln Ile
            165                 170                 175

Ala Ala Phe Arg Lys Glu Lys Glu Glu Lys Asp Gln Ala Leu Ser Gln
            180                 185                 190

Glu Leu Thr Asn Gln Phe Ile Lys Ala Ser Gln Lys Lys Glu Glu Gly
    195                 200                 205

Gly Ser Lys Ala Lys Ser Glu Ala Leu Lys Met Gly Arg Ala Ile Pro
    210                 215                 220

Asp His Glu Thr Ile Thr Gln Met Val Asp Val Glu Glu Glu Glu Ser
225                 230                 235                 240

Arg Leu Thr Phe Glu Gly Tyr Val Phe Asp Val Glu Ile Lys Ser Leu
            245                 250                 255

Arg Ser Asp Arg Lys Leu Leu Leu Phe Lys Met Thr Asp Tyr Ser Ser
            260                 265                 270

Ser Phe Leu Phe Lys Lys Phe Ser Asn Asn Ser Ser Asp Glu Ala Leu
    275                 280                 285
```

```
Phe Asp Gln Val Gln Glu Gly Met Trp Leu Lys Val Arg Gly Ser Val
    290             295             300

Gln Glu Asp Thr Phe Val Lys Asp Leu Val Val Met Ala Gln Asp Ile
305             310             315             320

Gln Glu Val Lys Lys Glu Pro Arg Arg Asp Leu Ala Lys Glu Gly Glu
                325             330             335

Lys Arg Val Glu Leu His Ala His Thr Thr Met Ser Gln Met Asp Gly
                340             345             350

Leu Val Pro Ala Lys Asp Leu Val Lys Gln Ala Ala Ala Phe Asp Gln
        355             360             365

Pro Ala Ile Ala Ile Thr Asp His Ala Val Val Gln Ser Phe Pro Glu
    370             375             380

Ala His Tyr Ala Gly Leu Asp Thr Gly Val Lys Ile Leu Tyr Gly Val
385             390             395             400

Glu Ala Asn Leu Val Ser Asp Gly Glu Leu Val Ala Tyr Asn Pro Ala
                405             410             415

Asp Ile Lys Leu Glu Glu Ala Thr Tyr Val Val Phe Asp Val Glu Thr
        420             425             430

Thr Gly Leu Ser Ala Arg Tyr Asp Gln Ile Ile Glu Leu Ala Ala Val
    435             440             445

Lys Met Glu Asn Gly Glu Ile Val Ser Glu Phe Gln Glu Phe Ile Asp
    450             455             460

Pro Gly Gln Pro Leu Ser Glu Thr Thr Thr Asn Leu Thr Gly Ile Thr
465             470             475             480

Asp Asp Met Val Gln Gly Ser Lys Ser Glu Asp Glu Val Leu His Ala
                485             490             495

Phe Gln Ala Phe Ser Glu Gly Thr Val Leu Val Ala His Asn Ala Ser
            500             505             510
```

Phe Asp Met Gly Phe Ile Asn Thr Ala Tyr Gln Arg His Gly Leu Gly
        515   520   525

Gln Ala Asp Gln Pro Val Ile Asp Thr Leu Glu Leu Ser Arg Met Leu
        530   535   540

His Pro Asn Leu Lys Ser His Arg Leu Asn Thr Leu Ala Lys Arg Tyr
545   550   555   560

Asp Val Ala Leu Glu His His His Arg Ala Ile Tyr Asp Ser Glu Ser
                565   570   575

Thr Ala Lys Leu Leu Trp Ile Phe Leu Lys Glu Ala Lys Asp Gln Tyr
                580   585   590

Asp Met Thr Ser His Gln Asp Leu Asn Ser Gln Val Gly Glu Gly Glu
        595   600   605

Ala Tyr Lys Gln Ala Arg Pro Thr His Ala Ser Ile Leu Val Lys Asn
        610   615   620

Gln Lys Gly Leu Lys Asn Leu Phe Lys Ile Val Ser His Ala His Val
625   630   635   640

Asn Tyr Phe Tyr Arg Val Pro Arg Ile Pro Lys Ser Ile Leu Ser Lys
                645   650   655

Tyr Arg Glu Gly Leu Leu Val Gly Ser Gly Cys Gly Gln Gly Glu Leu
                660   665   670

Phe Glu Ala Ile Met Gln Lys Gly Tyr Asp Glu Ala Leu Ala Val Ala
        675   680   685

Gln Asp Tyr Asp Tyr Ile Glu Val Met Pro Lys Ser Ala Tyr Ile Asp
        690   695   700

Leu Leu Asp Arg Asp Leu Ile Lys Asp Glu Ala Thr Leu Glu Glu Met
705   710   715   720

Ile Glu Asn Leu Val Lys Ile Gly His Glu Leu Asp Ile Pro Val Val
                725   730   735

Ala Thr Gly Asn Val His Tyr Leu Asn Pro Glu Asp Ala Val Leu Arg
            740   745   750

Asp Ile Leu Leu Glu Thr Ala Lys Lys Gly Ala Phe Ser Lys Ala Arg
            755   760   765

Asn Pro Glu Val His Phe Arg Thr Thr Asp Glu Met Leu Glu Glu Phe
    770   775   780

Ser Phe Leu Gly Gln Asp Gln Ala Tyr Glu Ile Val Val Thr Asn Thr
785   790   795   800

Gln Lys Ile Ala Asp Ser Ile Glu Ser Ile Ser Pro Val Lys Glu Gly
                805   810   815

Leu Tyr Ala Pro Lys Met Glu Gly Ser Asp Gln Glu Ile Arg Gln Met
            820   825   830

Ser Tyr Lys Gln Ala Lys Ala Leu Tyr Gly Asp Pro Leu Pro Ser Ile
            835   840   845

Val Glu Glu Arg Leu Glu Lys Glu Leu Lys Ser Ile Ile Asp Asn Asn
    850   855   860

Phe Ser Val Ile Tyr Leu Ile Ser Gln Lys Leu Val Lys Lys Ser Val
865   870   875   880

Glu Asp Gly Tyr Leu Val Gly Ser Arg Gly Ser Val Gly Ser Ser Phe
            885   890   895

Val Ala Thr Met Thr Gly Ile Thr Glu Val Asn Pro Leu Pro Pro His
            900   905   910

Tyr Arg Cys Pro Asn Cys Gln His Thr Glu Phe Phe Thr Asn Gly Glu
            915   920   925

Val Gly Ser Gly Phe Asp Leu Glu Ala Lys Lys Cys Pro Glu Cys Gln
    930   935   940

Ser Leu Met Glu Ser Asp Gly His Asp Ile Pro Phe Glu Thr Phe Leu
945   950   955   960

Gly Phe Asn Gly Asp Lys Val Pro Asp Ile Asp Leu Asn Phe Ser Gly

                          965   970   975

      Glu Tyr Gln Ala Lys Ala His Asn Tyr Thr Lys Val Leu Phe Gly Glu
              980   985   990

      Asp His Val Tyr Arg Ala Gly Thr Ile Thr Thr Ile Ala Asp Lys Thr
              995   1000   1005

      Ala Phe Gly Phe Val Lys Gly Tyr Glu Arg Asp Lys Gln Ile Asn Tyr
              1010   1015   1020

      Arg Ser Ala Glu Val Asp Arg Leu Ser Asp Gly Leu Thr Gly Val Arg
      1025   1030   1035   1040

      Arg Ser Thr Gly Gln His Pro Gly Gly Ile Ile Val Ile Pro Asp Asp
                     1045   1050   1055

      Met Asp Val Phe Asp Phe Thr Pro Ile Gln Tyr Pro Ala Asp Asp Gln
                     1060   1065   1070

      Thr Ala Glu Trp Gln Thr Thr His Phe Asp Phe His Ser Ile Asp Glu
                     1075   1080   1085

      Asn Val Leu Lys Leu Asp Ile Leu Gly His Asp Asp Pro Thr Met Ile
              1090   1095   1100

      Arg Lys Leu Gln Asp Leu Ser Gly Phe Asp Pro Gln Glu Ile Pro Val
      1105   1110   1115   1120

      Ser Asp Glu Asp Val Met Lys Ile Phe Ser Gly Pro Glu Val Leu Gly
                     1125   1130   1135

      Val Thr Pro Glu Gln Ile Phe Ser Asn Thr Gly Thr Leu Gly Val Pro
                     1140   1145   1150

      Glu Phe Gly Thr Gln Phe Val Arg Glu Met Leu Glu Gln Thr His Pro
              1155   1160   1165

      Ser Thr Phe Ala Glu Leu Leu Gln Ile Ser Gly Leu Ser His Gly Thr
              1170   1175   1180

      Asp Val Trp Leu Gly Asn Ala Glu Glu Leu Ile Arg Asn His Asn Ile
      1185   1190   1195   1200

Pro Leu Ser Glu Val Ile Gly Cys Arg Asp Asp Ile Met Val Tyr Leu
          1205   1210   1215

Gln His Gln Gly Leu Glu Asp Ser Leu Ala Phe Lys Ile Met Glu Phe
          1220   1225   1230

Val Arg Lys Gly Arg Gly Leu Gln Asp Asp Trp Ile Ala Thr Met Lys
          1235   1240   1245

Glu Asn Asp Val Pro Asp Trp Tyr Ile Glu Ser Cys Lys Lys Ile Lys
     1250   1255   1260

Tyr Met Phe Pro Lys Ala His Ala Ala Ala Tyr Val Leu Met Ala Leu
1265   1270   1275   1280

Arg Val Ala Tyr Phe Lys Val His Tyr Pro Leu Tyr Tyr Tyr Ala Ala
               1285   1290   1295

Tyr Phe Ser Ile Arg Ala Ser Asp Phe Asp Leu Ile Ala Met Val Lys
               1300   1305   1310

Gly Lys Glu Gly Ile Lys Gly Ala Met Lys Glu Ile Arg Asp Lys Glu
          1315   1320   1325

Arg Glu Lys Thr Ala Thr Ala Lys Asp Lys Ala Leu Leu Thr Val Leu
     1330   1335   1340

Glu Val Ala Asn Glu Met Val Glu Arg Gly Phe Asp Phe Lys Met Val
1345   1350   1355   1360

Asp Ile Asn Lys Ser Gln Ala Lys Asp Phe Val Ile Glu Asp Asn Gly
               1365   1370   1375

Leu Arg Ala Pro Phe Arg Ala Val Pro Ser Leu Gly Ser Ser Ala Ala
               1380   1385   1390

Gln Ala Val Ile Asp Ala Arg Glu Asp Ser Asp Phe Leu Ser Lys Glu
          1395   1400   1405

Asp Leu Ser Lys Arg Gly Lys Leu Ser Lys Thr Val Met Asp Tyr Leu
     1410   1415   1420

Asp Asn Asn His Val Leu Asp His Leu Pro Asp Glu Asn Gln Leu Ser
1425   1430   1435   1440

Leu Phe Asp Phe

<210> 71
<211> 1326
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (19)..(1326)
<223>

<400> 71
aagaaaggag gactcaat atg tct atg ttt gtc gac tac acc aaa gtt aac   51
                    Met Ser Met Phe Val Asp Tyr Thr Lys Val Asn
                    1   5   10

ctg aga gcc ggt aag ggc ggt gac gga atg gtg gct ttt aga cga gaa   99
Leu Arg Ala Gly Lys Gly Gly Asp Gly Met Val Ala Phe Arg Arg Glu
            15   20   25

aag tat gag ccc aat ggt gga cca gca ggc ggc gac ggt ggc agt ggc   147
Lys Tyr Glu Pro Asn Gly Gly Pro Ala Gly Gly Asp Gly Gly Ser Gly
        30   35   40

ggt aac att atc ttc aag gta gat gaa ggc ctc cgt acc ctg gta gac   195
Gly Asn Ile Ile Phe Lys Val Asp Glu Gly Leu Arg Thr Leu Val Asp
    45   50   55

ttc cgc tac aac ccc cat ttt aag gca gat agt ggc caa aat ggt atg   243
Phe Arg Tyr Asn Pro His Phe Lys Ala Asp Ser Gly Gln Asn Gly Met
60   65   70   75

ccc aag ggg atg aat ggt aag aag gca gag gac ttg att atc agt gtc   291
Pro Lys Gly Met Asn Gly Lys Lys Ala Glu Asp Leu Ile Ile Ser Val
                80   85   90

ccg cct gga acc att atc cgg gat gcc caa agt aag gct ata ctt gct   339
Pro Pro Gly Thr Ile Ile Arg Asp Ala Gln Ser Lys Ala Ile Leu Ala
                95   100   105

gac tta caa gaa gaa gga caa gaa gtc ttg gca gcc caa ggt ggc cgg   387
Asp Leu Gln Glu Glu Gly Gln Glu Val Leu Ala Ala Gln Gly Gly Arg
            110   115   120

gga ggt cgg ggc aat aaa cgt ttt gct acg cat aag aac cca gca ccc   435
Gly Gly Arg Gly Asn Lys Arg Phe Ala Thr His Lys Asn Pro Ala Pro
        125   130   135

tcc att gcc gaa aac ggc gag ccg ggc caa gag cgg gat gtc gaa ttg   483
Ser Ile Ala Glu Asn Gly Glu Pro Gly Gln Glu Arg Asp Val Glu Leu

```
            140                      145                      150                      155

            gaa tta aaa gtc atg gcc gat gtt ggc cta gtg ggt tat cct tct gtc          531
            Glu Leu Lys Val Met Ala Asp Val Gly Leu Val Gly Tyr Pro Ser Val
                        160                      165                      170

            ggg aaa tcg acc ctt ttg tcg gtt gtc tca ggc gct aaa ccc aaa att          579
            Gly Lys Ser Thr Leu Leu Ser Val Val Ser Gly Ala Lys Pro Lys Ile
                        175                      180                      185

            gga gcc tat cac ttt act aca ctt gcc cct aat tta ggt gta gtg aat          627
            Gly Ala Tyr His Phe Thr Thr Leu Ala Pro Asn Leu Gly Val Val Asn
                        190                      195                      200

            gca gtg gac ggc aag gaa ttt gtc ttg gcg gat att cct ggc tta att          675
            Ala Val Asp Gly Lys Glu Phe Val Leu Ala Asp Ile Pro Gly Leu Ile
                        205                      210                      215

            gaa ggg gct tca gaa ggg gtt ggt ttg ggg att gac ttc ctc aag cat          723
            Glu Gly Ala Ser Glu Gly Val Gly Leu Gly Ile Asp Phe Leu Lys His
            220                      225                      230                      235

            att gaa aga acc cgc atc ctc ctt cat gta ctt gat atg agc gga atg          771
            Ile Glu Arg Thr Arg Ile Leu Leu His Val Leu Asp Met Ser Gly Met
                        240                      245                      250

            gaa ggt cgc cat cca att gat gat ttt gac cag att aac caa gaa cta          819
            Glu Gly Arg His Pro Ile Asp Asp Phe Asp Gln Ile Asn Gln Glu Leu
                        255                      260                      265

            aaa gac tat aat gag aaa tta ttg gac cgc aag cag gtc att gtg gcc          867
            Lys Asp Tyr Asn Glu Lys Leu Leu Asp Arg Lys Gln Val Ile Val Ala
                        270                      275                      280

            aat aaa atg gac ctg ccc cag tcc cgg gat aat tta atc gaa ttt aaa          915
            Asn Lys Met Asp Leu Pro Gln Ser Arg Asp Asn Leu Ile Glu Phe Lys
                        285                      290                      295

            gcc gag tta gac agc cgg gac ctt gac tat gaa atc ttt gaa gtg tca          963
            Ala Glu Leu Asp Ser Arg Asp Leu Asp Tyr Glu Ile Phe Glu Val Ser
            300                      305                      310                      315

            gct gcc acc cag gct ggc att cag gac cta gtc atc cga cta gcc gac          1011
            Ala Ala Thr Gln Ala Gly Ile Gln Asp Leu Val Ile Arg Leu Ala Asp
                        320                      325                      330

            tta gtc gac caa ctg gac caa gcc cca agt tta gac cag gaa gaa act          1059
            Leu Val Asp Gln Leu Asp Gln Ala Pro Ser Leu Asp Gln Glu Glu Thr
                        335                      340                      345

            agt gaa gcc gac caa aga gtg gtc tac aag ttt caa gct gac caa gac          1107
            Ser Glu Ala Asp Gln Arg Val Val Tyr Lys Phe Gln Ala Asp Gln Asp
                        350                      355                      360

            aaa ttt gac ctt gac cgc gac cct gaa ggg gta tgg ttg gtt tct ggt          1155
            Lys Phe Asp Leu Asp Arg Asp Pro Glu Gly Val Trp Leu Val Ser Gly
                        365                      370                      375
```

```
ccc aag gtt gag cgt ttg tat gcc atg acc aat ttt gac cac gag gaa    1203
Pro Lys Val Glu Arg Leu Tyr Ala Met Thr Asn Phe Asp His Glu Glu
380                     385                 390                 395

gcc att atg cgg ttt tct cgc cag cta aga ggg atg gga gta gac caa    1251
Ala Ile Met Arg Phe Ser Arg Gln Leu Arg Gly Met Gly Val Asp Gln
                    400                 405                 410

gcc tta aga gac aag ggg gct cag tct ggt gac ctc gtc caa gtt gaa    1299
Ala Leu Arg Asp Lys Gly Ala Gln Ser Gly Asp Leu Val Gln Val Glu
            415                 420                 425

gat ttt gtc ttt gag ttc atg gat tag                                1326
Asp Phe Val Phe Glu Phe Met Asp
            430                 435
```

<210> 72
<211> 435
<212> PRT
<213> Alloiococcus otitidis

<400> 72

```
Met Ser Met Phe Val Asp Tyr Thr Lys Val Asn Leu Arg Ala Gly Lys
1               5                   10                  15

Gly Gly Asp Gly Met Val Ala Phe Arg Arg Glu Lys Tyr Glu Pro Asn
            20                  25                  30

Gly Gly Pro Ala Gly Gly Asp Gly Gly Ser Gly Gly Asn Ile Ile Phe
            35                  40                  45

Lys Val Asp Glu Gly Leu Arg Thr Leu Val Asp Phe Arg Tyr Asn Pro
    50                  55                  60

His Phe Lys Ala Asp Ser Gly Gln Asn Gly Met Pro Lys Gly Met Asn
65                  70                  75                  80

Gly Lys Lys Ala Glu Asp Leu Ile Ile Ser Val Pro Pro Gly Thr Ile
                85                  90                  95

Ile Arg Asp Ala Gln Ser Lys Ala Ile Leu Ala Asp Leu Gln Glu Glu
            100                 105                 110

Gly Gln Glu Val Leu Ala Ala Gln Gly Gly Arg Gly Gly Arg Gly Asn
        115                 120                 125

Lys Arg Phe Ala Thr His Lys Asn Pro Ala Pro Ser Ile Ala Glu Asn
```

```
              130                    135                    140
```

Gly Glu Pro Gly Gln Glu Arg Asp Val Glu Leu Glu Leu Lys Val Met
145   150   155   160

Ala Asp Val Gly Leu Val Gly Tyr Pro Ser Val Gly Lys Ser Thr Leu
            165   170   175

Leu Ser Val Val Ser Gly Ala Lys Pro Lys Ile Gly Ala Tyr His Phe
            180   185   190

Thr Thr Leu Ala Pro Asn Leu Gly Val Val Asn Ala Val Asp Gly Lys
            195   200   205

Glu Phe Val Leu Ala Asp Ile Pro Gly Leu Ile Glu Gly Ala Ser Glu
    210   215   220

Gly Val Gly Leu Gly Ile Asp Phe Leu Lys His Ile Glu Arg Thr Arg
225   230   235   240

Ile Leu Leu His Val Leu Asp Met Ser Gly Met Glu Gly Arg His Pro
            245   250   255

Ile Asp Asp Phe Asp Gln Ile Asn Gln Glu Leu Lys Asp Tyr Asn Glu
            260   265   270

Lys Leu Leu Asp Arg Lys Gln Val Ile Val Ala Asn Lys Met Asp Leu
    275   280   285

Pro Gln Ser Arg Asp Asn Leu Ile Glu Phe Lys Ala Glu Leu Asp Ser
    290   295   300

Arg Asp Leu Asp Tyr Glu Ile Phe Glu Val Ser Ala Ala Thr Gln Ala
305   310   315   320

Gly Ile Gln Asp Leu Val Ile Arg Leu Ala Asp Leu Val Asp Gln Leu
            325   330   335

Asp Gln Ala Pro Ser Leu Asp Gln Glu Glu Thr Ser Glu Ala Asp Gln
            340   345   350

Arg Val Val Tyr Lys Phe Gln Ala Asp Gln Asp Lys Phe Asp Leu Asp
    355   360   365

```
Arg Asp Pro Glu Gly Val Trp Leu Val Ser Gly Pro Lys Val Glu Arg
    370             375             380

Leu Tyr Ala Met Thr Asn Phe Asp His Glu Glu Ala Ile Met Arg Phe
385      .          390             395                     400

Ser Arg Gln Leu Arg Gly Met Gly Val Asp Gln Ala Leu Arg Asp Lys
                405             410                 415

Gly Ala Gln Ser Gly Asp Leu Val Gln Val Glu Asp Phe Val Phe Glu
                420             425             430

Phe Met Asp
        435
```

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<210> 73
<211> 1338
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (25)..(1338)
<223>

<400> 73
aagagaaaga aagaaggtgt actg atg gct aat cct tta gta gcc ata atc       51
                          Met Ala Asn Pro Leu Val Ala Ile Ile
                          1             5

ggc cgg cct aat gtc ggc aag tca act att ttc aac cgg att att gga       99
Gly Arg Pro Asn Val Gly Lys Ser Thr Ile Phe Asn Arg Ile Ile Gly
10                  15                  20              .       25

gac cgc tta gcc att gtc cag gat gaa ccc ggg gtc acc cgg gac cgt      147
Asp Arg Leu Ala Ile Val Gln Asp Glu Pro Gly Val Thr Arg Asp Arg
                30              35                  40

att tat gcc gat gct gaa tgg ttg ggc aaa gac ttt tct gtt ata gat      195
Ile Tyr Ala Asp Ala Glu Trp Leu Gly Lys Asp Phe Ser Val Ile Asp
                45              50                  55

acg gga gga atc act ttt gat gat ttg ccc ttg cat gaa gaa ata aaa      243
Thr Gly Gly Ile Thr Phe Asp Asp Leu Pro Leu His Glu Glu Ile Lys
            60              65              .70

gtc caa gct gaa att gcc att gat gaa gca gat gtc atc gtc atg gta      291
Val Gln Ala Glu Ile Ala Ile Asp Glu Ala Asp Val Ile Val Met Val
    75                  80                  85
```

```
acc agt gtc aaa gag ggc att aca gac ttg gat gac cag gta gcc tta    339
Thr Ser Val Lys Glu Gly Ile Thr Asp Leu Asp Asp Gln Val Ala Leu
90              95              100             105

att ttg cag cag tcc aac aaa ccc gtg gtc ctt gct gtt aat aaa aca    387
Ile Leu Gln Gln Ser Asn Lys Pro Val Val Leu Ala Val Asn Lys Thr
            110             115             120

gat aat cct gag ctt aga aat gaa ata tat gag ttt tac ggg tta ggc    435
Asp Asn Pro Glu Leu Arg Asn Glu Ile Tyr Glu Phe Tyr Gly Leu Gly
        125             130             135

ttg ggt gac ccc ctt ccg gta tcc ggg tct cac ggc cta ggc ttt ggg    483
Leu Gly Asp Pro Leu Pro Val Ser Gly Ser His Gly Leu Gly Phe Gly
        140             145             150

gac ctc tta gac gca gtg gtg gcc aac ttt cct aat gag gcc aat atg    531
Asp Leu Leu Asp Ala Val Val Ala Asn Phe Pro Asn Glu Ala Asn Met
    155             160             165

gct tat gac caa gat acc att aag ttc tgc ttg att ggt cgt ccc aat    579
Ala Tyr Asp Gln Asp Thr Ile Lys Phe Cys Leu Ile Gly Arg Pro Asn
170             175             180             185

gtt ggc aag tct agc cta gtt aat gct att att ggg gaa gac cgg gtt    627
Val Gly Lys Ser Ser Leu Val Asn Ala Ile Ile Gly Glu Asp Arg Val
            190             195             200

ata gtc tct gaa cta gaa ggg acc acc cgg gat gca att gac act ccc    675
Ile Val Ser Glu Leu Glu Gly Thr Thr Arg Asp Ala Ile Asp Thr Pro
            205             210             215

ttt atg acc cag gat ggc cag gac tat gtt atg atc gat act gct ggg    723
Phe Met Thr Gln Asp Gly Gln Asp Tyr Val Met Ile Asp Thr Ala Gly
        220             225             230

atc cgg cgt cgg ggc aag gtc tat gaa aaa act gaa aag tat tct gtt    771
Ile Arg Arg Arg Gly Lys Val Tyr Glu Lys Thr Glu Lys Tyr Ser Val
    235             240             245

atg cgg gca cag cga gct atc gac cgg tct gat gtg gtc ttg tgt gtc    819
Met Arg Ala Gln Arg Ala Ile Asp Arg Ser Asp Val Val Leu Cys Val
250             255             260             265

ctg gat gct gaa aca ggc att aga gac caa gat aag aag gtt ttc ggc    867
Leu Asp Ala Glu Thr Gly Ile Arg Asp Gln Asp Lys Lys Val Phe Gly
            270             275             280

tat gct cat caa gcc ggc aag gga att att att tta gtc aat aag tgg    915
Tyr Ala His Gln Ala Gly Lys Gly Ile Ile Ile Leu Val Asn Lys Trp
        285             290             295

gac acg att aaa aaa gag act aac acc atg cga gac ttt gag ttg caa    963
Asp Thr Ile Lys Lys Glu Thr Asn Thr Met Arg Asp Phe Glu Leu Gln
    300             305             310

att cgc gac caa ttc cgc tac ctc cac tat gcc cca atc ctt ttc gtc    1011
```

```
Ile Arg Asp Gln Phe Arg Tyr Leu His Tyr Ala Pro Ile Leu Phe Val
315             320             325
```

```
tca gcc aag acc aag cag aga ctg gaa gtc atc ccg gaa ttg gtc gac    1059
Ser Ala Lys Thr Lys Gln Arg Leu Glu Val Ile Pro Glu Leu Val Asp
330             335             340             345
```

```
cgg gtc tat tat aac cgc aat caa cgg gtc aag tcc tcc ctc tta aat    1107
Arg Val Tyr Tyr Asn Arg Asn Gln Arg Val Lys Ser Ser Leu Leu Asn
            350             355             360
```

```
gat gtg ctg agt gat gca cta gcc agc aat cct gca cct agt aag tca    1155
Asp Val Leu Ser Asp Ala Leu Ala Ser Asn Pro Ala Pro Ser Lys Ser
            365             370             375
```

```
ggg aag cga ctc aag gtc ttt tat gcg acc cag gta gcc act aat cca    1203
Gly Lys Arg Leu Lys Val Phe Tyr Ala Thr Gln Val Ala Thr Asn Pro
            380             385             390
```

```
cct act ttt gtg gtt ttt gtc aat gat cct gac ctc atg cac ttc tcc    1251
Pro Thr Phe Val Val Phe Val Asn Asp Pro Asp Leu Met His Phe Ser
            395             400             405
```

```
tat gag cgc ttt tta gaa aat cga ttc cgc gaa agc ttt gac ttc tat    1299
Tyr Glu Arg Phe Leu Glu Asn Arg Phe Arg Glu Ser Phe Asp Phe Tyr
410             415             420             425
```

```
ggc act ccg att cag ata atc cct aga gca agg aaa taa                1338
Gly Thr Pro Ile Gln Ile Ile Pro Arg Ala Arg Lys
            430             435
```

```
<210> 74
<211> 437
<212> PRT
<213> Alloiococcus otitidis
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<400> 74
Met Ala Asn Pro Leu Val Ala Ile Ile Gly Arg Pro Asn Val Gly Lys
1               5               10              15
```

```
Ser Thr Ile Phe Asn Arg Ile Ile Gly Asp Arg Leu Ala Ile Val Gln
            20              25              30
```

```
Asp Glu Pro Gly Val Thr Arg Asp Arg Ile Tyr Ala Asp Ala Glu Trp
            35              40              45
```

```
Leu Gly Lys Asp Phe Ser Val Ile Asp Thr Gly Gly Ile Thr Phe Asp
        50              55              60
```

```
Asp Leu Pro Leu His Glu Glu Ile Lys Val Gln Ala Glu Ile Ala Ile
65              70              75              80
```

Asp Glu Ala Asp Val Ile Val Met Val Thr Ser Val Lys Glu Gly Ile
                85   90   95

Thr Asp Leu Asp Asp Gln Val Ala Leu Ile Leu Gln Gln Ser Asn Lys
            100   105   110

Pro Val Val Leu Ala Val Asn Lys Thr Asp Asn Pro Glu Leu Arg Asn
        115   120   125

Glu Ile Tyr Glu Phe Tyr Gly Leu Gly Leu Gly Asp Pro Leu Pro Val
    130   135   140

Ser Gly Ser His Gly Leu Gly Phe Gly Asp Leu Leu Asp Ala Val Val
145   150   155   160

Ala Asn Phe Pro Asn Glu Ala Asn Met Ala Tyr Asp Gln Asp Thr Ile
            165   170   175

Lys Phe Cys Leu Ile Gly Arg Pro Asn Val Gly Lys Ser Ser Leu Val
            180   185   190

Asn Ala Ile Ile Gly Glu Asp Arg Val Ile Val Ser Glu Leu Glu Gly
        195   200   205

Thr Thr Arg Asp Ala Ile Asp Thr Pro Phe Met Thr Gln Asp Gly Gln
    210   215   220

Asp Tyr Val Met Ile Asp Thr Ala Gly Ile Arg Arg Arg Gly Lys Val
225   230   235   240

Tyr Glu Lys Thr Glu Lys Tyr Ser Val Met Arg Ala Gln Arg Ala Ile
            245   250   255

Asp Arg Ser Asp Val Val Leu Cys Val Leu Asp Ala Glu Thr Gly Ile
            260   265   270

Arg Asp Gln Asp Lys Lys Val Phe Gly Tyr Ala His Gln Ala Gly Lys
        275   280   285

Gly Ile Ile Ile Leu Val Asn Lys Trp Asp Thr Ile Lys Lys Glu Thr
    290   295   300

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Asn Thr Met Arg Asp Phe Glu Leu Gln Ile Arg Asp Gln Phe Arg Tyr
305               310               315               320


Leu His Tyr Ala Pro Ile Leu Phe Val Ser Ala Lys Thr Lys Gln Arg
                325               330               335


Leu Glu Val Ile Pro Glu Leu Val Asp Arg Val Tyr Tyr Asn Arg Asn
                340               345               350


Gln Arg Val Lys Ser Ser Leu Leu Asn Asp Val Leu Ser Asp Ala Leu
            355               360               365


Ala Ser Asn Pro Ala Pro Ser Lys Ser Gly Lys Arg Leu Lys Val Phe
    370               375               380


Tyr Ala Thr Gln Val Ala Thr Asn Pro Pro Thr Phe Val Val Phe Val
385               390               395               400


Asn Asp Pro Asp Leu Met His Phe Ser Tyr Glu Arg Phe Leu Glu Asn
                405               410               415


Arg Phe Arg Glu Ser Phe Asp Phe Tyr Gly Thr Pro Ile Gln Ile Ile
            420               425               430


Pro Arg Ala Arg Lys
            435


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<213> Alloiococcus otitidis

<220>
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<223>

<400> 75
aataaaaga ttg aaa caa ata tgt ctt aga cga aga ggt gac aag atg act      51
          Met Lys Gln Ile Cys Leu Arg Arg Arg Gly Asp Lys Met Thr
          1               5                   10


ttt acc cac tta caa gtg acc agt gct tac acc ttg atg gct tcg acc      99
Phe Thr His Leu Gln Val Thr Ser Ala Tyr Thr Leu Met Ala Ser Thr
15               20               25               30


atc caa ttg ccc ctc ctg atg gac cgc ctg aag gag ctt ggc atg gag     147
Ile Gln Leu Pro Leu Leu Met Asp Arg Leu Lys Glu Leu Gly Met Glu
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              35                    40                    45

gct gtt gcc ttg acc gac cac aat gtt atg cat gga gcg gtc gaa ttt      195
Ala Val Ala Leu Thr Asp His Asn Val Met His Gly Ala Val Glu Phe
            50                    55                    60

tac caa gaa gcc aaa aag cat ggc att aaa ccc att atg gga cta cgg      243
Tyr Gln Glu Ala Lys Lys His Gly Ile Lys Pro Ile Met Gly Leu Arg
            65                    70                    75

gct gac cta gac gaa gga ata acc gtc acc ctc ctg gct aaa aac aag      291
Ala Asp Leu Asp Glu Gly Ile Thr Val Thr Leu Leu Ala Lys Asn Lys
            80                    85                    90

gct ggc tac cag gct ctc tta gcc tta tcg act gac ctt caa gtt aac      339
Ala Gly Tyr Gln Ala Leu Leu Ala Leu Ser Thr Asp Leu Gln Val Asn
95                   100                   105                   110

aag cag gct att aca ctt gac caa gtc cgt tct gtg gcc cag gac ctc      387
Lys Gln Ala Ile Thr Leu Asp Gln Val Arg Ser Val Ala Gln Asp Leu
                115                   120                   125

tat aca ata ttc cca agc tct gac cca aaa gtg aaa gca gac ctc tta      435
Tyr Thr Ile Phe Pro Ser Ser Asp Pro Lys Val Lys Ala Asp Leu Leu
                130                   135                   140

gat aag cag gca agc aat ttg acc gcg atg act cag aac ctg ccc cat      483
Asp Lys Gln Ala Ser Asn Leu Thr Ala Met Thr Gln Asn Leu Pro His
            145                   150                   155

tca tat ttg ggt ctg gtg cca gac caa gat caa aaa att tac cag tta      531
Ser Tyr Leu Gly Leu Val Pro Asp Gln Asp Gln Lys Ile Tyr Gln Leu
            160                   165                   170

gcc cgg acc ttg tca gat tct gga ggt ttg aaa gtc tta gcc tta tct      579
Ala Arg Thr Leu Ser Asp Ser Gly Gly Leu Lys Val Leu Ala Leu Ser
175                   180                   185                   190

gac gtc cgt tgc ttg gaa gaa agc caa gtc tcc act ttg gaa atc tta      627
Asp Val Arg Cys Leu Glu Glu Ser Gln Val Ser Thr Leu Glu Ile Leu
                195                   200                   205

agc cac atc aaa gcc aac cag aaa att caa ttt gac acc cag gct cgg      675
Ser His Ile Lys Ala Asn Gln Lys Ile Gln Phe Asp Thr Gln Ala Arg
                210                   215                   220

gaa aat tat gcc ctg cgc agt ccc caa gaa atg gag tct ttt ttt aac      723
Glu Asn Tyr Ala Leu Arg Ser Pro Gln Glu Met Glu Ser Phe Phe Asn
                225                   230                   235

cag gtg ggt tta ggt cag gcc ctt aaa aat act aaa gat gta gcc cag      771
Gln Val Gly Leu Gly Gln Ala Leu Lys Asn Thr Lys Asp Val Ala Gln
            240                   245                   250

tca gta gac tgg tcc ctg gac ctc ggt cag gct aaa ttg cct gca ttt      819
Ser Val Asp Trp Ser Leu Asp Leu Gly Gln Ala Lys Leu Pro Ala Phe
255                   260                   265                   270
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gac ctg ccg gaa ggg gag acc aag gac tcc tac ctt ggc aag ctt gcc     867
Asp Leu Pro Glu Gly Glu Thr Lys Asp Ser Tyr Leu Gly Lys Leu Ala
            275                 280                 285

caa aaa gga ctc caa gaa cgg gtt cca ggc tac ggc caa gac tac caa     915
Gln Lys Gly Leu Gln Glu Arg Val Pro Gly Tyr Gly Gln Asp Tyr Gln
            290                 295                 300

gac cgt cta gac aag gaa cta gcg gtt att tct tcc atg ggc ttt tcg     963
Asp Arg Leu Asp Lys Glu Leu Ala Val Ile Ser Ser Met Gly Phe Ser
            305                 310                 315

gac tac ttc ctg att gtt tgg gac ctg atg caa ttt gcc cgc cag gaa    1011
Asp Tyr Phe Leu Ile Val Trp Asp Leu Met Gln Phe Ala Arg Gln Glu
            320                 325                 330

aaa att gag act ggt ttt ggc cgg ggg tca gct gcc gct tct ttg gta    1059
Lys Ile Glu Thr Gly Phe Gly Arg Gly Ser Ala Ala Ala Ser Leu Val
335                 340                 345                 350

tct tat gcc ctc tac att acg ggg gta gat ccc atc cat tat gac ctc    1107
Ser Tyr Ala Leu Tyr Ile Thr Gly Val Asp Pro Ile His Tyr Asp Leu
            355                 360                 365

ctc ttt gaa cgt ttt ttg aac aag gac cgc ttt acc atg cct gat att    1155
Leu Phe Glu Arg Phe Leu Asn Lys Asp Arg Phe Thr Met Pro Asp Ile
            370                 375                 380

gac cta gac ttc cca gac aac aag cgc cag gtc atc ttg gac tat gtc    1203
Asp Leu Asp Phe Pro Asp Asn Lys Arg Gln Val Ile Leu Asp Tyr Val
            385                 390                 395

tac cgg aag tat ggt cct gac cat gtg gcc caa att ttg acc ttt ggg    1251
Tyr Arg Lys Tyr Gly Pro Asp His Val Ala Gln Ile Leu Thr Phe Gly
            400                 405                 410

acc ttt gcg gct aag tcc tcc atc agg gaa att atg cgg acc ttg ggt    1299
Thr Phe Ala Ala Lys Ser Ser Ile Arg Glu Ile Met Arg Thr Leu Gly
415                 420                 425                 430

tac aag aat gaa gac atg aag acc tgg tcc cag gcc ata cca gat acc    1347
Tyr Lys Asn Glu Asp Met Lys Thr Trp Ser Gln Ala Ile Pro Asp Thr
            435                 440                 445

gtc aac atc agc ttg tca aag gcc tat gac gag tcg aaa gac ctt caa    1395
Val Asn Ile Ser Leu Ser Lys Ala Tyr Asp Glu Ser Lys Asp Leu Gln
            450                 455                 460

aaa ctg gtc cag caa agc cat gaa aat gag cgg atc ttt gcc atg gcc    1443
Lys Leu Val Gln Gln Ser His Glu Asn Glu Arg Ile Phe Ala Met Ala
            465                 470                 475

cag gat atc gaa ggc ctg cca agg aac tat tca acc cat gcg gcc ggt    1491
Gln Asp Ile Glu Gly Leu Pro Arg Asn Tyr Ser Thr His Ala Ala Gly
            480                 485                 490
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gtc gtc atg tca gac cag ccc cta atc cat tcc ctt ccc cta caa gat      1539
Val Val Met Ser Asp Gln Pro Leu Ile His Ser Leu Pro Leu Gln Asp
495             500             505             510

ggc aac gga aag gtc ccc aac acc caa ttt acc atg gag gat gtt gaa      1587
Gly Asn Gly Lys Val Pro Asn Thr Gln Phe Thr Met Glu Asp Val Glu
                515             520             525

gcg gtc ggc tta ctc aag atg gac ttt ttg agt tta aaa aat tta acc      1635
Ala Val Gly Leu Leu Lys Met Asp Phe Leu Ser Leu Lys Asn Leu Thr
            530             535             540

atc cta gca gac tgc ttg aac ttt agc cag tat gaa ggg cag gga ggg      1683
Ile Leu Ala Asp Cys Leu Asn Phe Ser Gln Tyr Glu Gly Gln Gly Gly
            545             550             555

ggt ata agt aaa caa gat ata cca atc gac gac cct aag acc ctg gat      1731
Gly Ile Ser Lys Gln Asp Ile Pro Ile Asp Asp Pro Lys Thr Leu Asp
        560             565             570

ctt ttt gcc cgg gga gac aca aat ggg gtc ttc caa ttt gaa aaa gag      1779
Leu Phe Ala Arg Gly Asp Thr Asn Gly Val Phe Gln Phe Glu Lys Glu
575             580             585             590

gga atc aaa aaa gtc ctc cgc cag ctt caa ccc act tct ttt gaa gat      1827
Gly Ile Lys Lys Val Leu Arg Gln Leu Gln Pro Thr Ser Phe Glu Asp
            595             600             605

atc gtc gcc acc aac gcc ctc tac cgc ccc ggt ccc atg ggg caa att      1875
Ile Val Ala Thr Asn Ala Leu Tyr Arg Pro Gly Pro Met Gly Gln Ile
            610             615             620

gag aat tat att aac cgt aaa cat ggt caa gaa aaa att atc tac ccc      1923
Glu Asn Tyr Ile Asn Arg Lys His Gly Gln Glu Lys Ile Ile Tyr Pro
        625             630             635

cat gaa gac tta aag gac atc ctt gaa gtc act tat ggc att att gtc      1971
His Glu Asp Leu Lys Asp Ile Leu Glu Val Thr Tyr Gly Ile Ile Val
        640             645             650

tac cag gaa caa gtc atg cag gta gct acc caa cta gct ggc tat agt      2019
Tyr Gln Glu Gln Val Met Gln Val Ala Thr Gln Leu Ala Gly Tyr Ser
655             660             665             670

ttg tcg gaa gct gac caa ttg cgg cgg act atg tcc aaa aaa atc cag      2067
Leu Ser Glu Ala Asp Gln Leu Arg Arg Thr Met Ser Lys Lys Ile Gln
            675             680             685

tca gaa atg gac cag gga cgg gaa aaa ttt ata aga gga gcc ttg gac      2115
Ser Glu Met Asp Gln Gly Arg Glu Lys Phe Ile Arg Gly Ala Leu Asp
            690             695             700

aag ggc tac agt gag tca gta gcc cga gag gtt tat aac tat att gca      2163
Lys Gly Tyr Ser Glu Ser Val Ala Arg Glu Val Tyr Asn Tyr Ile Ala
            705             710             715

aag ttt gct aac tac ggc ttt aac cgt gcc cat gct gtt gcc tac tcc      2211
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```
      Lys Phe Ala Asn Tyr Gly Phe Asn Arg Ala His Ala Val Ala Tyr Ser
          720             725             730

atg ctt gcc tac cat atg gcc tac ttt aag gtc cac cag cct aaa tct    2259
Met Leu Ala Tyr His Met Ala Tyr Phe Lys Val His Gln Pro Lys Ser
735             740             745             750

ttt ttt gcg gct gtg atg aag gca gac tgg ggt aac aag gct aaa att    2307
Phe Phe Ala Ala Val Met Lys Ala Asp Trp Gly Asn Lys Ala Lys Ile
            755             760             765

tac aag tat gcc cat gaa gtc cgg gct aga aaa att aaa cta cta aaa    2355
Tyr Lys Tyr Ala His Glu Val Arg Ala Arg Lys Ile Lys Leu Leu Lys
                770             775             780

cca gac atc aac caa agc ctt gga tct ttt acg gtt cgg cag aat ggc    2403
Pro Asp Ile Asn Gln Ser Leu Gly Ser Phe Thr Val Arg Gln Asn Gly
            785             790             795

att caa gtg ggg ctt aag atg gtc aag ggg gtg gct agc ccc ttt gtc    2451
Ile Gln Val Gly Leu Lys Met Val Lys Gly Val Ala Ser Pro Phe Val
        800             805             810

aac cac atc ctt gaa att cgg aaa gaa aag gga gct ttt acc agc ctg    2499
Asn His Ile Leu Glu Ile Arg Lys Glu Lys Gly Ala Phe Thr Ser Leu
815             820             825             830

cgt gac ttt tgt gaa aaa att gac agc caa ttc tta agt caa gac ccc    2547
Arg Asp Phe Cys Glu Lys Ile Asp Ser Gln Phe Leu Ser Gln Asp Pro
            835             840             845

att gaa gca ttg att ttg gtg ggg gcc ttt gac caa atg ggc cct aat    2595
Ile Glu Ala Leu Ile Leu Val Gly Ala Phe Asp Gln Met Gly Pro Asn
            850             855             860

cgg cgg acc atg tta gcg ggc ttg gaa gca acg att gaa ttc gtg gcc    2643
Arg Arg Thr Met Leu Ala Gly Leu Glu Ala Thr Ile Glu Phe Val Ala
            865             870             875

aaa agt tcg ggc aat atc acc ctt ttt gac act ctc aag ccc cgc caa    2691
Lys Ser Ser Gly Asn Ile Thr Leu Phe Asp Thr Leu Lys Pro Arg Gln
        880             885             890

gaa gac ctg gaa gag ttt agc cca aag gac ctc att caa tat gaa gaa    2739
Glu Asp Leu Glu Glu Phe Ser Pro Lys Asp Leu Ile Gln Tyr Glu Glu
895             900             905             910

gaa tta acc ggt ttt tac ttc tcc agc cac ccc ttg agc cgg tat gac    2787
Glu Leu Thr Gly Phe Tyr Phe Ser Ser His Pro Leu Ser Arg Tyr Asp
                915             920             925

tcc ctg cga cag gac tta aaa acg tcc ttt ata gct gat tta gaa gag    2835
Ser Leu Arg Gln Asp Leu Lys Thr Ser Phe Ile Ala Asp Leu Glu Glu
            930             935             940

ggc caa tct tgc caa gtt tta ggt cag ctg gtt caa gtc cgg aaa act    2883
Gly Gln Ser Cys Gln Val Leu Gly Gln Leu Val Gln Val Arg Lys Thr
```

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        945                      950                      955

cag act aga aac caa caa ccc atg gcc ttt gtt agc ctg gct gac caa    2931
Gln Thr Arg Asn Gln Gln Pro Met Ala Phe Val Ser Leu Ala Asp Gln
    960                  965                  970

aca gga caa att agc ctg gtg gtc ttt ccg aat gta tac cgc gaa tgc    2979
Thr Gly Gln Ile Ser Leu Val Val Phe Pro Asn Val Tyr Arg Glu Cys
975                  980                  985                  990

cta cct tac ctc aaa gaa gga gtg gtc ctg gtc gtc tca ggc aag gta    3027
Leu Pro Tyr Leu Lys Glu Gly Val Val Leu Val Val Ser Gly Lys Val
                995                  1000                 1005

gaa gtt agg aag gga gaa atc cag cta aaa gtc cag acc atg aaa gag    3075
Glu Val Arg Lys Gly Glu Ile Gln Leu Lys Val Gln Thr Met Lys Glu
            1010                 1015                 1020

gcc agc cag gtc caa aaa gag act aag cag ctt tac ctg aaa ttt gct    3123
Ala Ser Gln Val Gln Lys Glu Thr Lys Gln Leu Tyr Leu Lys Phe Ala
        1025                 1030                 1035

gac ttg aac caa gat aaa gaa agt ttt cgt caa gtg caa aag atc ttg    3171
Asp Leu Asn Gln Asp Lys Glu Ser Phe Arg Gln Val Gln Lys Ile Leu
    1040                 1045                 1050

gcc cga cat ccc ggc cag aag cga gtg att gtt tac gac cag gcc agc    3219
Ala Arg His Pro Gly Gln Lys Arg Val Ile Val Tyr Asp Gln Ala Ser
1055                 1060                 1065                 1070

cag caa gca ctc cag ctc aaa gca aaa ttt aat ttc gac gga cgg acg    3267
Gln Gln Ala Leu Gln Leu Lys Ala Lys Phe Asn Phe Asp Gly Arg Thr
                1075                 1080                 1085

gat acc cta aac cag ctc cag gac ctc cta ggc cag gat tct tgt atc    3315
Asp Thr Leu Asn Gln Leu Gln Asp Leu Leu Gly Gln Asp Ser Cys Ile
            1090                 1095                 1100

tta aaa taa                                                        3324
Leu Lys
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<210> 76
<211> 1104
<212> PRT
<213> Alloiococcus otitidis

<400> 76

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Met Lys Gln Ile Cys Leu Arg Arg Arg Gly Asp Lys Met Thr Phe Thr
1               5               10              15


His Leu Gln Val Thr Ser Ala Tyr Thr Leu Met Ala Ser Thr Ile Gln
            20              25              30


Leu Pro Leu Leu Met Asp Arg Leu Lys Glu Leu Gly Met Glu Ala Val
```

35   40   45

Ala Leu Thr Asp His Asn Val Met His Gly Ala Val Glu Phe Tyr Gln
    50   55   60

Glu Ala Lys Lys His Gly Ile Lys Pro Ile Met Gly Leu Arg Ala Asp
65   70   75   80

Leu Asp Glu Gly Ile Thr Val Thr Leu Leu Ala Lys Asn Lys Ala Gly
            85   90   95

Tyr Gln Ala Leu Leu Ala Leu Ser Thr Asp Leu Gln Val Asn Lys Gln
            100   105   110

Ala Ile Thr Leu Asp Gln Val Arg Ser Val Ala Gln Asp Leu Tyr Thr
        115   120   125

Ile Phe Pro Ser Ser Asp Pro Lys Val Lys Ala Asp Leu Leu Asp Lys
    130   135   140

Gln Ala Ser Asn Leu Thr Ala Met Thr Gln Asn Leu Pro His Ser Tyr
145   150   155   160

Leu Gly Leu Val Pro Asp Gln Asp Gln Lys Ile Tyr Gln Leu Ala Arg
            165   170   175

Thr Leu Ser Asp Ser Gly Gly Leu Lys Val Leu Ala Leu Ser Asp Val
            180   185   190

Arg Cys Leu Glu Glu Ser Gln Val Ser Thr Leu Glu Ile Leu Ser His
        195   200   205

Ile Lys Ala Asn Gln Lys Ile Gln Phe Asp Thr Gln Ala Arg Glu Asn
    210   215   220

Tyr Ala Leu Arg Ser Pro Gln Glu Met Glu Ser Phe Phe Asn Gln Val
225   230   235   240

Gly Leu Gly Gln Ala Leu Lys Asn Thr Lys Asp Val Ala Gln Ser Val
            245   250   255

Asp Trp Ser Leu Asp Leu Gly Gln Ala Lys Leu Pro Ala Phe Asp Leu
            260   265   270

```
Pro Glu Gly Glu Thr Lys Asp Ser Tyr Leu Gly Lys Leu Ala Gln Lys
    275             280             285

Gly Leu Gln Glu Arg Val Pro Gly Tyr Gly Gln Asp Tyr Gln Asp Arg
    290             295             300

Leu Asp Lys Glu Leu Ala Val Ile Ser Ser Met Gly Phe Ser Asp Tyr
305             310             315             320

Phe Leu Ile Val Trp Asp Leu Met Gln Phe Ala Arg Gln Glu Lys Ile
            325             330             335

Glu Thr Gly Phe Gly Arg Gly Ser Ala Ala Ala Ser Leu Val Ser Tyr
            340             345             350

Ala Leu Tyr Ile Thr Gly Val Asp Pro Ile His Tyr Asp Leu Leu Phe
        355             360             365

Glu Arg Phe Leu Asn Lys Asp Arg Phe Thr Met Pro Asp Ile Asp Leu
    370             375             380

Asp Phe Pro Asp Asn Lys Arg Gln Val Ile Leu Asp Tyr Val Tyr Arg
385             390             395             400

Lys Tyr Gly Pro Asp His Val Ala Gln Ile Leu Thr Phe Gly Thr Phe
            405             410             415

Ala Ala Lys Ser Ser Ile Arg Glu Ile Met Arg Thr Leu Gly Tyr Lys
            420             425             430

Asn Glu Asp Met Lys Thr Trp Ser Gln Ala Ile Pro Asp Thr Val Asn
    435             440             445

Ile Ser Leu Ser Lys Ala Tyr Asp Glu Ser Lys Asp Leu Gln Lys Leu
    450             455             460

Val Gln Gln Ser His Glu Asn Glu Arg Ile Phe Ala Met Ala Gln Asp
465             470             475             480

Ile Glu Gly Leu Pro Arg Asn Tyr Ser Thr His Ala Ala Gly Val Val
            485             490             495
```

```
Met Ser Asp Gln Pro Leu Ile His Ser Leu Pro Leu Gln Asp Gly Asn
            500                 505                 510


Gly Lys Val Pro Asn Thr Gln Phe Thr Met Glu Asp Val Glu Ala Val
            515                 520                 525


Gly Leu Leu Lys Met Asp Phe Leu Ser Leu Lys Asn Leu Thr Ile Leu
    530                 535                 540


Ala Asp Cys Leu Asn Phe Ser Gln Tyr Glu Gly Gln Gly Gly Gly Ile
545                 550                 555                 560


Ser Lys Gln Asp Ile Pro Ile Asp Asp Pro Lys Thr Leu Asp Leu Phe
                565                 570                 575


Ala Arg Gly Asp Thr Asn Gly Val Phe Gln Phe Glu Lys Glu Gly Ile
            580                 585                 590


Lys Lys Val Leu Arg Gln Leu Gln Pro Thr Ser Phe Glu Asp Ile Val
    595                 600                 605


Ala Thr Asn Ala Leu Tyr Arg Pro Gly Pro Met Gly Gln Ile Glu Asn
    610                 615                 620


Tyr Ile Asn Arg Lys His Gly Gln Glu Lys Ile Ile Tyr Pro His Glu
625                 630                 635                 640


Asp Leu Lys Asp Ile Leu Glu Val Thr Tyr Gly Ile Ile Val Tyr Gln
            645                 650                 655


Glu Gln Val Met Gln Val Ala Thr Gln Leu Ala Gly Tyr Ser Leu Ser
            660                 665                 670


Glu Ala Asp Gln Leu Arg Arg Thr Met Ser Lys Lys Ile Gln Ser Glu
    675                 680                 685


Met Asp Gln Gly Arg Glu Lys Phe Ile Arg Gly Ala Leu Asp Lys Gly
    690                 695                 700


Tyr Ser Glu Ser Val Ala Arg Glu Val Tyr Asn Tyr Ile Ala Lys Phe
705                 710                 715                 720
```

Ala Asn Tyr Gly Phe Asn Arg Ala His Ala Val Ala Tyr Ser Met Leu
            725   730   735

Ala Tyr His Met Ala Tyr Phe Lys Val His Gln Pro Lys Ser Phe Phe
            740   745   750

Ala Ala Val Met Lys Ala Asp Trp Gly Asn Lys Ala Lys Ile Tyr Lys
            755   760   765

Tyr Ala His Glu Val Arg Ala Arg Lys Ile Lys Leu Leu Lys Pro Asp
    770   775   780

Ile Asn Gln Ser Leu Gly Ser Phe Thr Val Arg Gln Asn Gly Ile Gln
785   790   795   800

Val Gly Leu Lys Met Val Lys Gly Val Ala Ser Pro Phe Val Asn His
            805   810   815

Ile Leu Glu Ile Arg Lys Glu Lys Gly Ala Phe Thr Ser Leu Arg Asp
            820   825   830

Phe Cys Glu Lys Ile Asp Ser Gln Phe Leu Ser Gln Asp Pro Ile Glu
            835   840   845

Ala Leu Ile Leu Val Gly Ala Phe Asp Gln Met Gly Pro Asn Arg Arg
    850   855   860

Thr Met Leu Ala Gly Leu Glu Ala Thr Ile Glu Phe Val Ala Lys Ser
865   870   875   880

Ser Gly Asn Ile Thr Leu Phe Asp Thr Leu Lys Pro Arg Gln Glu Asp
            885   890   895

Leu Glu Glu Phe Ser Pro Lys Asp Leu Ile Gln Tyr Glu Glu Glu Leu
            900   905   910

Thr Gly Phe Tyr Phe Ser Ser His Pro Leu Ser Arg Tyr Asp Ser Leu
            915   920   925

Arg Gln Asp Leu Lys Thr Ser Phe Ile Ala Asp Leu Glu Glu Gly Gln
    930   935   940

Ser Cys Gln Val Leu Gly Gln Leu Val Gln Val Arg Lys Thr Gln Thr

```
945                 950                 955                 960


Arg Asn Gln Gln Pro Met Ala Phe Val Ser Leu Ala Asp Gln Thr Gly
                965                 970                 975


Gln Ile Ser Leu Val Val Phe Pro Asn Val Tyr Arg Glu Cys Leu Pro
                980                 985                 990


Tyr Leu Lys Glu Gly Val Val Leu Val Val Ser Gly Lys Val Glu Val
            995                 1000                1005


Arg Lys Gly Glu Ile Gln Leu Lys Val Gln Thr Met Lys Glu Ala Ser
    1010                1015                1020


Gln Val Gln Lys Glu Thr Lys Gln Leu Tyr Leu Lys Phe Ala Asp Leu
1025                1030                1035                1040


Asn Gln Asp Lys Glu Ser Phe Arg Gln Val Gln Lys Ile Leu Ala Arg
            1045                1050                1055


His Pro Gly Gln Lys Arg Val Ile Val Tyr Asp Gln Ala Ser Gln Gln
        1060                1065                1070


Ala Leu Gln Leu Lys Ala Lys Phe Asn Phe Asp Gly Arg Thr Asp Thr
        1075                1080                1085


Leu Asn Gln Leu Gln Asp Leu Leu Gly Gln Asp Ser Cys Ile Leu Lys
    1090                1095                1100
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<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (7)..(1212)
<223>

<400> 77
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acaaag atg ctg aaa aat aaa aag ata gcc tta tat gtt act ggt ggt        48
       Met Leu Lys Asn Lys Lys Ile Ala Leu Tyr Val Thr Gly Gly
        1                5                   10
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```
ata gca gta tac aaa tca ctt tac tta ctt agg gaa atc atc aaa caa        96
Ile Ala Val Tyr Lys Ser Leu Tyr Leu Leu Arg Glu Ile Ile Lys Gln
15                  20                  25                  30

ggc ggg gag gtc cgg gtt gcc atg act caa gca gct tgt caa ttt gtt       144
Gly Gly Glu Val Arg Val Ala Met Thr Gln Ala Ala Cys Gln Phe Val
                35                  40                  45

aac ccc tta tct ttt cag gtt tta agc caa aaa aag gtt cag att gac       192
Asn Pro Leu Ser Phe Gln Val Leu Ser Gln Lys Lys Val Gln Ile Asp
                50                  55                  60

act ttt gaa gaa ggt cag ccc gaa tcg gtc agt cac att gat ttg acg       240
Thr Phe Glu Glu Gly Gln Pro Glu Ser Val Ser His Ile Asp Leu Thr
                65                  70                  75

gat tgg gcc gac tac tcc atc gtg gct ccg gca act gcc aat atc atc       288
Asp Trp Ala Asp Tyr Ser Ile Val Ala Pro Ala Thr Ala Asn Ile Ile
                80                  85                  90

ggc aag ctg gcc aat ggg att ggg gac gat ttt gtt tca aca gcc ttg       336
Gly Lys Leu Ala Asn Gly Ile Gly Asp Asp Phe Val Ser Thr Ala Leu
95                  100                 105                 110

ttg gca acg gac cac ccc att ttt tta gtc cca gcc atg aac acc aag       384
Leu Ala Thr Asp His Pro Ile Phe Leu Val Pro Ala Met Asn Thr Lys
                115                 120                 125

atg tat gaa aat ccc gct ctt aag aaa aac aag gcc ttc ctt att gaa       432
Met Tyr Glu Asn Pro Ala Leu Lys Lys Asn Lys Ala Phe Leu Ile Glu
                130                 135                 140

cag ggc cat tac tgg atg gag ccg gat att gga ttt tta gca gag ggc       480
Gln Gly His Tyr Trp Met Glu Pro Asp Ile Gly Phe Leu Ala Glu Gly
                145                 150                 155

tac gaa ggc ttg ggt cgt ttt cca gac cta gac cgg att atg gcg gaa       528
Tyr Glu Gly Leu Gly Arg Phe Pro Asp Leu Asp Arg Ile Met Ala Glu
160                 165                 170

ttt aac cat ttt att att gct agg aat cca ggt atc cta tca gga aaa       576
Phe Asn His Phe Ile Ile Ala Arg Asn Pro Gly Ile Leu Ser Gly Lys
175                 180                 185                 190

aaa gtc ctc gtc aca gca ggt ggg acg gtg gag cgg att gat ccc gtc       624
Lys Val Leu Val Thr Ala Gly Gly Thr Val Glu Arg Ile Asp Pro Val
                195                 200                 205

cgg tat att tcc aat gat tct tct ggt aag atg ggc cac caa ctt gct       672
Arg Tyr Ile Ser Asn Asp Ser Ser Gly Lys Met Gly His Gln Leu Ala
                210                 215                 220

caa gcg gcc tat gaa gct ggg gcc cag gtt agc ttg gta aca gcc agt       720
Gln Ala Ala Tyr Glu Ala Gly Ala Gln Val Ser Leu Val Thr Ala Ser
                225                 230                 235

gac ttg ccg acc agt ccc ttt att gac cgc ttt cag gtg gag tcc acc       768
```

```
Asp Leu Pro Thr Ser Pro Phe Ile Asp Arg Phe Gln Val Glu Ser Thr
    240             245             250

tta gac ttg tac caa aca gtt agt gac ctc tat gac cac cat gac att      816
Leu Asp Leu Tyr Gln Thr Val Ser Asp Leu Tyr Asp His His Asp Ile
255             260             265             270

ctc atg atg gcc gca gcg gtg tct gac tac cgg cca gtc aac cgg tca      864
Leu Met Met Ala Ala Ala Val Ser Asp Tyr Arg Pro Val Asn Arg Ser
                275             280             285

gac aaa aag atg aaa aag caa gat aat tta acc att gaa ctg gaa aaa      912
Asp Lys Lys Met Lys Lys Gln Asp Asn Leu Thr Ile Glu Leu Glu Lys
                290             295             300

aat cct gat att ttg gcc gaa atg ggc cgg cgg aaa gac caa caa atc      960
Asn Pro Asp Ile Leu Ala Glu Met Gly Arg Arg Lys Asp Gln Gln Ile
            305             310             315

aat gtc ggc ttt gca gca gaa acc cat aac ctt gaa gaa tat gcc caa     1008
Asn Val Gly Phe Ala Ala Glu Thr His Asn Leu Glu Glu Tyr Ala Gln
        320             325             330

aaa aaa tta gcc tcc aaa caa gct gac ttg atc gta gcc aat gaa gtg     1056
Lys Lys Leu Ala Ser Lys Gln Ala Asp Leu Ile Val Ala Asn Glu Val
335             340             345             350

ggc cgg gga gac cgg ggc ttt aat gcg gat gaa aat gcg gcc ctt gtt     1104
Gly Arg Gly Asp Arg Gly Phe Asn Ala Asp Glu Asn Ala Ala Leu Val
                355             360             365

ttt tcc agt gac caa gat ccg ctt gag ctt ccc ctt cag tct aaa aaa     1152
Phe Ser Ser Asp Gln Asp Pro Leu Glu Leu Pro Leu Gln Ser Lys Lys
            370             375             380

gat atg gca aaa aag att att gaa gtg gtg gcc agt aaa ttg cct gct     1200
Asp Met Ala Lys Lys Ile Ile Glu Val Val Ala Ser Lys Leu Pro Ala
        385             390             395

tct ccc aaa taa                                                      1212
Ser Pro Lys
        400
```

```
<210> 78
<211> 401
<212> PRT
<213> Alloiococcus otitidis

<400> 78
Met Leu Lys Asn Lys Lys Ile Ala Leu Tyr Val Thr Gly Gly Ile Ala
1               5               10              15


Val Tyr Lys Ser Leu Tyr Leu Leu Arg Glu Ile Ile Lys Gln Gly Gly
            20              25              30
```

```
Glu Val Arg Val Ala Met Thr Gln Ala Ala Cys Gln Phe Val Asn Pro
        35              40              45

Leu Ser Phe Gln Val Leu Ser Gln Lys Lys Val Gln Ile Asp Thr Phe
    50              55              60

Glu Glu Gly Gln Pro Glu Ser Val Ser His Ile Asp Leu Thr Asp Trp
65              70              75              80

Ala Asp Tyr Ser Ile Val Ala Pro Ala Thr Ala Asn Ile Ile Gly Lys
            85              90              95

Leu Ala Asn Gly Ile Gly Asp Asp Phe Val Ser Thr Ala Leu Leu Ala
            100             105             110

Thr Asp His Pro Ile Phe Leu Val Pro Ala Met Asn Thr Lys Met Tyr
        115             120             125

Glu Asn Pro Ala Leu Lys Lys Asn Lys Ala Phe Leu Ile Glu Gln Gly
    130             135             140

His Tyr Trp Met Glu Pro Asp Ile Gly Phe Leu Ala Glu Gly Tyr Glu
145             150             155             160

Gly Leu Gly Arg Phe Pro Asp Leu Asp Arg Ile Met Ala Glu Phe Asn
            165             170             175

His Phe Ile Ile Ala Arg Asn Pro Gly Ile Leu Ser Gly Lys Lys Val
            180             185             190

Leu Val Thr Ala Gly Gly Thr Val Glu Arg Ile Asp Pro Val Arg Tyr
        195             200             205

Ile Ser Asn Asp Ser Ser Gly Lys Met Gly His Gln Leu Ala Gln Ala
    210             215             220

Ala Tyr Glu Ala Gly Ala Gln Val Ser Leu Val Thr Ala Ser Asp Leu
225             230             235             240

Pro Thr Ser Pro Phe Ile Asp Arg Phe Gln Val Glu Ser Thr Leu Asp
            245             250             255
```

```
Leu Tyr Gln Thr Val Ser Asp Leu Tyr Asp His His Asp Ile Leu Met
        260             265             270


Met Ala Ala Ala Val Ser Asp Tyr Arg Pro Val Asn Arg Ser Asp Lys
        275             280             285


Lys Met Lys Lys Gln Asp Asn Leu Thr Ile Glu Leu Glu Lys Asn Pro
        290             295             300


Asp Ile Leu Ala Glu Met Gly Arg Arg Lys Asp Gln Gln Ile Asn Val
305             310             315             320


Gly Phe Ala Ala Glu Thr His Asn Leu Glu Glu Tyr Ala Gln Lys Lys
                325             330             335


Leu Ala Ser Lys Gln Ala Asp Leu Ile Val Ala Asn Glu Val Gly Arg
            340             345             350


Gly Asp Arg Gly Phe Asn Ala Asp Glu Asn Ala Ala Leu Val Phe Ser
            355             360             365


Ser Asp Gln Asp Pro Leu Glu Leu Pro Leu Gln Ser Lys Lys Asp Met
    370             375             380


Ala Lys Lys Ile Ile Glu Val Val Ala Ser Lys Leu Pro Ala Ser Pro
385             390             395             400


Lys
```

```
<210> 79
<211> 1053
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (22)..(1053)
<223>

<400> 79
aagaagaagg gaggaagact g atg aaa att gaa gac caa ctc aaa aaa att          51
                         Met Lys Ile Glu Asp Gln Leu Lys Lys Ile
                         1               5               10

aaa gac caa gac ttg tct ccc ctc tac ctg gtc cag gga gat gac cag          99
Lys Asp Gln Asp Leu Ser Pro Leu Tyr Leu Val Gln Gly Asp Asp Gln
            15              20              25
```

```
tac ttg tta gac cag gtt aaa aaa agt ttg agc cag gcc ctt ttg gac     147
Tyr Leu Leu Asp Gln Val Lys Lys Ser Leu Ser Gln Ala Leu Leu Asp
            30              35              40

cag gat gaa gct tct atg aat ttt ggt caa ttt aat atg atg gct gat     195
Gln Asp Glu Ala Ser Met Asn Phe Gly Gln Phe Asn Met Met Ala Asp
            45              50              55

agc cta gac atg gcc ttg tct gat gcg gaa tcc tat ccc ttt ttt ggg     243
Ser Leu Asp Met Ala Leu Ser Asp Ala Glu Ser Tyr Pro Phe Phe Gly
        60              65              70

gac aag cgc ctg gtt tac atc caa gac ccc ttt ttc cta aca ggg gag     291
Asp Lys Arg Leu Val Tyr Ile Gln Asp Pro Phe Phe Leu Thr Gly Glu
75              80              85              90

aag cgg aaa aca gat ctg gac cat gac ttg gat cgc ttg ctg gct tac     339
Lys Arg Lys Thr Asp Leu Asp His Asp Leu Asp Arg Leu Leu Ala Tyr
                95              100             105

ctc caa aac cca gcc gac ttt act gtt ctc gtc ttc ttt gcc ccc tat     387
Leu Gln Asn Pro Ala Asp Phe Thr Val Leu Val Phe Phe Ala Pro Tyr
            110             115             120

gag aaa ctg gac aag cgg aag aag gtc acc aaa gcc cta ttg cag gaa     435
Glu Lys Leu Asp Lys Arg Lys Lys Val Thr Lys Ala Leu Leu Gln Glu
            125             130             135

gct gag att ata gat gcc agt tcc cca gac caa aga gat cta aaa gat     483
Ala Glu Ile Ile Asp Ala Ser Ser Pro Asp Gln Arg Asp Leu Lys Asp
        140             145             150

atg gtc cag aaa aaa gta aag gct cga ggc tac cag ttt gac aaa gga     531
Met Val Gln Lys Lys Val Lys Ala Arg Gly Tyr Gln Phe Asp Lys Gly
155             160             165             170

gct tta aag gcc ctg gtt gaa aaa acc aat gcc aac tta agt cgg gtc     579
Ala Leu Lys Ala Leu Val Glu Lys Thr Asn Ala Asn Leu Ser Arg Val
            175             180             185

atg caa gag ttg gac aag tta ttc ttg tac cat tta gat gac aaa atc     627
Met Gln Glu Leu Asp Lys Leu Phe Leu Tyr His Leu Asp Asp Lys Ile
            190             195             200

atc acc gtc cag tca gtt gac cag gtc gta tca cca agc ctg gaa agt     675
Ile Thr Val Gln Ser Val Asp Gln Val Val Ser Pro Ser Leu Glu Ser
            205             210             215

aat gtc ttt agt att aac gac tat att tta agc ggg caa agc cag gct     723
Asn Val Phe Ser Ile Asn Asp Tyr Ile Leu Ser Gly Gln Ser Gln Ala
            220             225             230

gct ata cgg gcc ttt aat gac tta att caa caa aag gaa gag cca att     771
Ala Ile Arg Ala Phe Asn Asp Leu Ile Gln Gln Lys Glu Glu Pro Ile
235             240             245             250
```

```
aaa atc atc gcc att atg atg aac caa ttc cgt tta tta ttg cag gtt        819
Lys Ile Ile Ala Ile Met Met Asn Gln Phe Arg Leu Leu Leu Gln Val
                255                 260                 265

aaa ata ttg cgg act aag ggc tac caa caa gga gag atc gct aaa atc        867
Lys Ile Leu Arg Thr Lys Gly Tyr Gln Gln Gly Glu Ile Ala Lys Ile
                270                 275                 280

tta aaa gtt cac ccc tac cgg gtt aag cta gcc ata gag aaa cag gag        915
Leu Lys Val His Pro Tyr Arg Val Lys Leu Ala Ile Glu Lys Gln Glu
                285                 290                 295

att ttt tcc aag caa agt cta tcg acc gcc tac cgc tac tta att gag        963
Ile Phe Ser Lys Gln Ser Leu Ser Thr Ala Tyr Arg Tyr Leu Ile Glu
                300                 305                 310

tca gat cat ttg att aaa acg ggc aag gtg acc tcg caa ttg caa ttt       1011
Ser Asp His Leu Ile Lys Thr Gly Lys Val Thr Ser Gln Leu Gln Phe
315                 320                 325                 330

gaa ctt ttt gcc cta caa ttt aaa gat tct gtc atg aat taa             1053
Glu Leu Phe Ala Leu Gln Phe Lys Asp Ser Val Met Asn
                335                 340
```

<210> 80
<211> 343
<212> PRT
<213> Alloiococcus otitidis

<400> 80
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Met Lys Ile Glu Asp Gln Leu Lys Lys Ile Lys Asp Gln Asp Leu Ser
1               5                   10                  15


Pro Leu Tyr Leu Val Gln Gly Asp Asp Gln Tyr Leu Leu Asp Gln Val
                20                  25                  30


Lys Lys Ser Leu Ser Gln Ala Leu Leu Asp Gln Asp Glu Ala Ser Met
                35                  40                  45


Asn Phe Gly Gln Phe Asn Met Met Ala Asp Ser Leu Asp Met Ala Leu
    50                  55                  60


Ser Asp Ala Glu Ser Tyr Pro Phe Phe Gly Asp Lys Arg Leu Val Tyr
65                  70                  75                  80


Ile Gln Asp Pro Phe Phe Leu Thr Gly Glu Lys Arg Lys Thr Asp Leu
                85                  90                  95


Asp His Asp Leu Asp Arg Leu Leu Ala Tyr Leu Gln Asn Pro Ala Asp
                100                 105                 110
```

```
Phe Thr Val Leu Val Phe Phe Ala Pro Tyr Glu Lys Leu Asp Lys Arg
        115             120             125

Lys Lys Val Thr Lys Ala Leu Leu Gln Glu Ala Glu Ile Ile Asp Ala
    130             135             140

Ser Ser Pro Asp Gln Arg Asp Leu Lys Asp Met Val Gln Lys Lys Val
145             150             155             160

Lys Ala Arg Gly Tyr Gln Phe Asp Lys Gly Ala Leu Lys Ala Leu Val
            165             170             175

Glu Lys Thr Asn Ala Asn Leu Ser Arg Val Met Gln Glu Leu Asp Lys
        180             185             190

Leu Phe Leu Tyr His Leu Asp Asp Lys Ile Ile Thr Val Gln Ser Val
        195             200             205

Asp Gln Val Val Ser Pro Ser Leu Glu Ser Asn Val Phe Ser Ile Asn
    210             215             220

Asp Tyr Ile Leu Ser Gly Gln Ser Gln Ala Ala Ile Arg Ala Phe Asn
225             230             235             240

Asp Leu Ile Gln Gln Lys Glu Glu Pro Ile Lys Ile Ile Ala Ile Met
            245             250             255

Met Asn Gln Phe Arg Leu Leu Leu Gln Val Lys Ile Leu Arg Thr Lys
            260             265             270

Gly Tyr Gln Gln Gly Glu Ile Ala Lys Ile Leu Lys Val His Pro Tyr
            275             280             285

Arg Val Lys Leu Ala Ile Glu Lys Gln Glu Ile Phe Ser Lys Gln Ser
        290             295             300

Leu Ser Thr Ala Tyr Arg Tyr Leu Ile Glu Ser Asp His Leu Ile Lys
305             310             315             320

Thr Gly Lys Val Thr Ser Gln Leu Gln Phe Glu Leu Phe Ala Leu Gln
            325             330             335
```

Phe Lys Asp Ser Val Met Asn
              340

<210> 81
<211> 477
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (1)..(477)
<223>

<400> 81

```
atg aat cgc gca atc tat gca ggc agt ttt gat ccg att acc ctg ggc      48
Met Asn Arg Ala Ile Tyr Ala Gly Ser Phe Asp Pro Ile Thr Leu Gly
1               5                   10                  15

cac ctg gat atc att aaa agg gcc agc cac tta ttc gat gaa gtc atc      96
His Leu Asp Ile Ile Lys Arg Ala Ser His Leu Phe Asp Glu Val Ile
            20                  25                  30

gtt gca gtt gct aat aat aca tcg aaa aat agt atg ttg aac ttt gac     144
Val Ala Val Ala Asn Asn Thr Ser Lys Asn Ser Met Leu Asn Phe Asp
        35                  40                  45

caa aaa ttg aac ctg gtt gaa caa tca att gct agc cag ggt cta gct     192
Gln Lys Leu Asn Leu Val Glu Gln Ser Ile Ala Ser Gln Gly Leu Ala
    50                  55                  60

aat gtt caa gcc aag aca tta gag tca ggc ttg att gtt gac ttt gct     240
Asn Val Gln Ala Lys Thr Leu Glu Ser Gly Leu Ile Val Asp Phe Ala
65                  70                  75                  80

aag gac caa gga gct agt agt ctg gtt agg ggg ttg cgg tcg gtt aaa     288
Lys Asp Gln Gly Ala Ser Ser Leu Val Arg Gly Leu Arg Ser Val Lys
                85                  90                  95

gac ttt gaa tat gag att gcc att gag gac tta aat aag gtc caa gac     336
Asp Phe Glu Tyr Glu Ile Ala Ile Glu Asp Leu Asn Lys Val Gln Asp
                100                 105                 110

cca gct att gaa aca gtt tac cta gtc tcg tct tcc aaa tac cgg tcc     384
Pro Ala Ile Glu Thr Val Tyr Leu Val Ser Ser Ser Lys Tyr Arg Ser
            115                 120                 125

att tct tcc tct att gtt cgg gaa att att aag ttt aat ggc cgg ctt     432
Ile Ser Ser Ser Ile Val Arg Glu Ile Ile Lys Phe Asn Gly Arg Leu
        130                 135                 140

gat gac cta gta cct gac ccc gtc gtc gaa tat ttt aaa aaa taa        477
Asp Asp Leu Val Pro Asp Pro Val Val Glu Tyr Phe Lys Lys
145                 150                 155
```

<210> 82
<211> 158
<212> PRT
<213> Alloiococcus otitidis

<400> 82
Met Asn Arg Ala Ile Tyr Ala Gly Ser Phe Asp Pro Ile Thr Leu Gly
1   5   10   15

His Leu Asp Ile Ile Lys Arg Ala Ser His Leu Phe Asp Glu Val Ile
            20   25   30

Val Ala Val Ala Asn Asn Thr Ser Lys Asn Ser Met Leu Asn Phe Asp
        35   40   45

Gln Lys Leu Asn Leu Val Glu Gln Ser Ile Ala Ser Gln Gly Leu Ala
    50   55   60

Asn Val Gln Ala Lys Thr Leu Glu Ser Gly Leu Ile Val Asp Phe Ala
65   70   75   80

Lys Asp Gln Gly Ala Ser Ser Leu Val Arg Gly Leu Arg Ser Val Lys
                85   90   95

Asp Phe Glu Tyr Glu Ile Ala Ile Glu Asp Leu Asn Lys Val Gln Asp
            100   105   110

Pro Ala Ile Glu Thr Val Tyr Leu Val Ser Ser Ser Lys Tyr Arg Ser
        115   120   125

Ile Ser Ser Ser Ile Val Arg Glu Ile Ile Lys Phe Asn Gly Arg Leu
    130   135   140

Asp Asp Leu Val Pro Asp Pro Val Val Glu Tyr Phe Lys Lys
145   150   155

<210> 83
<211> 1260
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (28)..(1260)
<223>

<400> 83

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ataaggattt caggaggaat actcata atg gat ttc aac tta gat aat aca gtt        54
                                 Met Asp Phe Asn Leu Asp Asn Thr Val
                                 1               5

tca ggt ggc gca aag att aag gtt att ggt gtt ggc ggt gct ggt ggc         102
Ser Gly Gly Ala Lys Ile Lys Val Ile Gly Val Gly Gly Ala Gly Gly
10              15              20              25

aat gcc gtt aac cgg atg att gaa gat gga gtc gaa ggc gtt gaa ttt         150
Asn Ala Val Asn Arg Met Ile Glu Asp Gly Val Glu Gly Val Glu Phe
                30              35              40

att gta gcc aat aca gat gtc caa gcc ctt gat gcc aac cga gct gag         198
Ile Val Ala Asn Thr Asp Val Gln Ala Leu Asp Ala Asn Arg Ala Glu
            45              50              55

act aaa att caa ctc gga gag aag tta acc agg gga ctc ggt gcc gga         246
Thr Lys Ile Gln Leu Gly Glu Lys Leu Thr Arg Gly Leu Gly Ala Gly
            60              65              70

gct aat cca gaa gtt ggc cgt aag tcg gct gaa gag agt gaa gaa acc         294
Ala Asn Pro Glu Val Gly Arg Lys Ser Ala Glu Glu Ser Glu Glu Thr
        75              80              85

att gcc gaa gct ctt gaa gga gct gac atg gtc ttc gtt act gct ggt         342
Ile Ala Glu Ala Leu Glu Gly Ala Asp Met Val Phe Val Thr Ala Gly
90              95              100             105

atg ggt ggc ggt act ggt act ggc ggg gcg ggc att att gcc cgc att         390
Met Gly Gly Gly Thr Gly Thr Gly Gly Ala Gly Ile Ile Ala Arg Ile
                110             115             120

gcc aaa gaa caa ggg gct ttg act gta ggg gtt att acc cgg ccg ttc         438
Ala Lys Glu Gln Gly Ala Leu Thr Val Gly Val Ile Thr Arg Pro Phe
            125             130             135

act ttt gaa gga cca aaa cgt ggg cgc ttt gca gcc gaa ggg att gcc         486
Thr Phe Glu Gly Pro Lys Arg Gly Arg Phe Ala Ala Glu Gly Ile Ala
        140             145             150

caa atg cgg gaa cat gtt gac acc ctt gtc acc atc tcc aac aac cgc         534
Gln Met Arg Glu His Val Asp Thr Leu Val Thr Ile Ser Asn Asn Arg
        155             160             165

ttg cta gaa att gtg gac aag aaa aca ccg atg atg gaa gcc ttc aga         582
Leu Leu Glu Ile Val Asp Lys Lys Thr Pro Met Met Glu Ala Phe Arg
170             175             180             185

gaa gca gat aat gtc ctc cgc caa ggg gtt caa ggt ata tct gac ttg         630
Glu Ala Asp Asn Val Leu Arg Gln Gly Val Gln Gly Ile Ser Asp Leu
                190             195             200

att acc aat cca ggc tac gtc aac tta gac ttt gcc gat gtc aaa acg         678
Ile Thr Asn Pro Gly Tyr Val Asn Leu Asp Phe Ala Asp Val Lys Thr
            205             210             215

gtg atg gcc aac caa ggt tct gcc ttg atg ggg att ggg tct gct tca         726
```

```
Val Met Ala Asn Gln Gly Ser Ala Leu Met Gly Ile Gly Ser Ala Ser
    220                 225             230

ggt gag aat aga acg gct gaa gct act aag aaa gct att tca tct cca      774
Gly Glu Asn Arg Thr Ala Glu Ala Thr Lys Lys Ala Ile Ser Ser Pro
    235                 240             245

ctt ttg gaa gtc tcc ctc aat ggg gct gaa aat gtc cta tta aac ata      822
Leu Leu Glu Val Ser Leu Asn Gly Ala Glu Asn Val Leu Leu Asn Ile
250                 255             260             265

acc gga aac caa gac tta acc ctc ttt gaa gct caa gat gct tct gat      870
Thr Gly Asn Gln Asp Leu Thr Leu Phe Glu Ala Gln Asp Ala Ser Asp
            270             275             280

atc gtc ggg gct gct gct tct ggt gat gtt aat att atc ttc ggt act      918
Ile Val Gly Ala Ala Ala Ser Gly Asp Val Asn Ile Ile Phe Gly Thr
            285             290             295

tcc atc aat gaa gac ctg gaa gat gag gtc atc gtt acc gtt att gca      966
Ser Ile Asn Glu Asp Leu Glu Asp Glu Val Ile Val Thr Val Ile Ala
            300             305             310

act ggt atc act ggt aaa gac atg ggc gag aaa tct tct aaa tcc tca     1014
Thr Gly Ile Thr Gly Lys Asp Met Gly Glu Lys Ser Ser Lys Ser Ser
    315                 320             325

aac cgt agc caa ggt cct agt caa aaa agt caa gct cga tca gct agt     1062
Asn Arg Ser Gln Gly Pro Ser Gln Lys Ser Gln Ala Arg Ser Ala Ser
330                 335             340             345

gag tct agc ttc tct agc tgg caa aac caa tcc aat gaa aga cca ggg     1110
Glu Ser Ser Phe Ser Ser Trp Gln Asn Gln Ser Asn Glu Arg Pro Gly
                350             355             360

gaa gac caa gac cga cca agc tct caa aga cgg gaa gtc gat cgg tcc     1158
Glu Asp Gln Asp Arg Pro Ser Ser Gln Arg Arg Glu Val Asp Arg Ser
            365             370             375

gaa aac ctg ttc aat gac gat agt aag gac cag cca gca gac tct ggt     1206
Glu Asn Leu Phe Asn Asp Asp Ser Lys Asp Gln Pro Ala Asp Ser Gly
            380             385             390

gat gat gac gaa ttg gat acc cct cct ttc ttt aga cgt cgc cgc aag     1254
Asp Asp Asp Glu Leu Asp Thr Pro Pro Phe Phe Arg Arg Arg Arg Lys
    395             400             405

aat tag                                                             1260
Asn
410
```

<210> 84
<211> 410
<212> PRT
<213> Alloiococcus otitidis

<400> 84

Met Asp Phe Asn Leu Asp Asn Thr Val Ser Gly Gly Ala Lys Ile Lys
1   5   10   15

Val Ile Gly Val Gly Gly Ala Gly Gly Asn Ala Val Asn Arg Met Ile
            20   25   30

Glu Asp Gly Val Glu Gly Val Glu Phe Ile Val Ala Asn Thr Asp Val
        35   40   45

Gln Ala Leu Asp Ala Asn Arg Ala Glu Thr Lys Ile Gln Leu Gly Glu
    50   55   60

Lys Leu Thr Arg Gly Leu Gly Ala Gly Ala Asn Pro Glu Val Gly Arg
65   70   75   80

Lys Ser Ala Glu Glu Ser Glu Glu Thr Ile Ala Glu Ala Leu Glu Gly
            85   90   95

Ala Asp Met Val Phe Val Thr Ala Gly Met Gly Gly Gly Thr Gly Thr
            100   105   110

Gly Gly Ala Gly Ile Ile Ala Arg Ile Ala Lys Glu Gln Gly Ala Leu
        115   120   125

Thr Val Gly Val Ile Thr Arg Pro Phe Thr Phe Glu Gly Pro Lys Arg
    130   135   140

Gly Arg Phe Ala Ala Glu Gly Ile Ala Gln Met Arg Glu His Val Asp
145   150   155   160

Thr Leu Val Thr Ile Ser Asn Asn Arg Leu Leu Glu Ile Val Asp Lys
                165   170   175

Lys Thr Pro Met Met Glu Ala Phe Arg Glu Ala Asp Asn Val Leu Arg
            180   185   190

Gln Gly Val Gln Gly Ile Ser Asp Leu Ile Thr Asn Pro Gly Tyr Val
        195   200   205

Asn Leu Asp Phe Ala Asp Val Lys Thr Val Met Ala Asn Gln Gly Ser
    210   215   220

Ala Leu Met Gly Ile Gly Ser Ala Ser Gly Glu Asn Arg Thr Ala Glu
225   230   235   240

Ala Thr Lys Lys Ala Ile Ser Ser Pro Leu Leu Glu Val Ser Leu Asn
                245   250   255

Gly Ala Glu Asn Val Leu Leu Asn Ile Thr Gly Asn Gln Asp Leu Thr
            260   265   270

Leu Phe Glu Ala Gln Asp Ala Ser Asp Ile Val Gly Ala Ala Ala Ser
        275   280   285

Gly Asp Val Asn Ile Ile Phe Gly Thr Ser Ile Asn Glu Asp Leu Glu
    290   295   300

Asp Glu Val Ile Val Thr Val Ile Ala Thr Gly Ile Thr Gly Lys Asp
305   310   315   320

Met Gly Glu Lys Ser Ser Lys Ser Ser Asn Arg Ser Gln Gly Pro Ser
            325   330   335

Gln Lys Ser Gln Ala Arg Ser Ala Ser Glu Ser Ser Phe Ser Ser Trp
            340   345   350

Gln Asn Gln Ser Asn Glu Arg Pro Gly Glu Asp Gln Asp Arg Pro Ser
            355   360   365

Ser Gln Arg Arg Glu Val Asp Arg Ser Glu Asn Leu Phe Asn Asp Asp
    370   375   380

Ser Lys Asp Gln Pro Ala Asp Ser Gly Asp Asp Asp Glu Leu Asp Thr
385   390   395   400

Pro Pro Phe Phe Arg Arg Arg Arg Lys Asn
                405   410

<210> 85
<211> 1377
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (13)..(1377)
<223>

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<400> 85
acagataata ga atg ttt tta gat atg gag gtt tca atg aat atg aaa aat       51
              Met Phe Leu Asp Met Glu Val Ser Met Asn Met Lys Asn
              1              5                10


ggg gtt tat aca agc ctt gat att gga acc act tca ata aaa gta gtt        99
Gly Val Tyr Thr Ser Leu Asp Ile Gly Thr Thr Ser Ile Lys Val Val
    15              20                25


gtc agt gaa gtt gat aat aat cag ctc aaa gtt att gga gta gga aaa      147
Val Ser Glu Val Asp Asn Asn Gln Leu Lys Val Ile Gly Val Gly Lys
30              35              40                  45


gct caa tca aaa ggt tta aaa agg ggc atg gtt gtc gat ata gat gct      195
Ala Gln Ser Lys Gly Leu Lys Arg Gly Met Val Val Asp Ile Asp Ala
                50              55                60


acc gtc cag gcc att cat act gca gtg aag cag gct gct gat aag act      243
Thr Val Gln Ala Ile His Thr Ala Val Lys Gln Ala Ala Asp Lys Thr
                65              70              75


ggt gtt atg atc aac cag ctc att gtt gga gtt cct gct aat ggt gtt      291
Gly Val Met Ile Asn Gln Leu Ile Val Gly Val Pro Ala Asn Gly Val
            80              85              90


agt att gaa ccc tgt cac ggg gtc att act gta gat gac cgg tcc aag      339
Ser Ile Glu Pro Cys His Gly Val Ile Thr Val Asp Asp Arg Ser Lys
95              100             105


gaa ata gac agc cag gaa gtg aac cgg gta gtc aac cag tcc att gct      387
Glu Ile Asp Ser Gln Glu Val Asn Arg Val Val Asn Gln Ser Ile Ala
110             115             120             125


aat atc gtt ccg cca gat aga gac tta tta tcc gtc agt tta gaa gaa      435
Asn Ile Val Pro Pro Asp Arg Asp Leu Leu Ser Val Ser Leu Glu Glu
                130             135             140


ttt att gta gat ggt ttt gat gaa att cat gat ccg aga ggc atg gtg      483
Phe Ile Val Asp Gly Phe Asp Glu Ile His Asp Pro Arg Gly Met Val
            145             150             155


ggc cag cgg tta gaa ctt tac ggg aca gca att tca gtg cct aaa aca      531
Gly Gln Arg Leu Glu Leu Tyr Gly Thr Ala Ile Ser Val Pro Lys Thr
            160             165             170


att tta cat aac att aga cgt tgt gtt gaa aaa gcg ggc tat caa att      579
Ile Leu His Asn Ile Arg Arg Cys Val Glu Lys Ala Gly Tyr Gln Ile
    175             180             185


gct gcc tta att ctc cag ccc caa gcc atg gcc aag gta gcc ttg tct      627
Ala Ala Leu Ile Leu Gln Pro Gln Ala Met Ala Lys Val Ala Leu Ser
190             195             200             205


gag gat gag cgg aat ttt ggt aca gtt atg gtg gat ata ggc gga ggt      675
Glu Asp Glu Arg Asn Phe Gly Thr Val Met Val Asp Ile Gly Gly Gly
            210             215             220
```

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caa acg acc cta tca gcc att cac gat gag caa gtg aag tat gcc aat     723
Gln Thr Thr Leu Ser Ala Ile His Asp Glu Gln Val Lys Tyr Ala Asn
            225                 230                 235

gtg gtc caa gaa gcc gga gaa tat att acc aaa gac att tcc att gtc     771
Val Val Gln Glu Ala Gly Glu Tyr Ile Thr Lys Asp Ile Ser Ile Val
            240                 245                 250

atc aac acc tca cag caa aat gca gaa aag ctc aaa aga gaa gtt ggg     819
Ile Asn Thr Ser Gln Gln Asn Ala Glu Lys Leu Lys Arg Glu Val Gly
        255                 260                 265

gcc att aaa agt cag tct gat tca act gtt caa gta gat gtt gta ggt     867
Ala Ile Lys Ser Gln Ser Asp Ser Thr Val Gln Val Asp Val Val Gly
270                 275                 280                 285

caa aat gaa cct gtg aag att aaa gaa tcc tat gtc ggt gaa att att     915
Gln Asn Glu Pro Val Lys Ile Lys Glu Ser Tyr Val Gly Glu Ile Ile
                290                 295                 300

gaa gcc cgg gtt agc caa atc ttt gaa aaa gtg aag gct gac ctt gac     963
Glu Ala Arg Val Ser Gln Ile Phe Glu Lys Val Lys Ala Asp Leu Asp
            305                 310                 315

cca att aac gcc ttc caa ttg cca ggt ggt gcc gtt att tcc ggc ggt    1011
Pro Ile Asn Ala Phe Gln Leu Pro Gly Gly Ala Val Ile Ser Gly Gly
            320                 325                 330

tca gct gcc ata cca ggt att gac agc ttg gct gaa gac atc ttc aag    1059
Ser Ala Ala Ile Pro Gly Ile Asp Ser Leu Ala Glu Asp Ile Phe Lys
335                 340                 345

gtt cgg tca gag ctc tac att ccc gac tac atg ggt atc cga act ccc    1107
Val Arg Ser Glu Leu Tyr Ile Pro Asp Tyr Met Gly Ile Arg Thr Pro
350                 355                 360                 365

gcc ttc act gtg gca gtc ggc ttg acc ctc tac caa gcc cag act tct    1155
Ala Phe Thr Val Ala Val Gly Leu Thr Leu Tyr Gln Ala Gln Thr Ser
                370                 375                 380

gat att gag cgg gcc atc aac cag tcc atc ttg caa aat atc ggt att    1203
Asp Ile Glu Arg Ala Ile Asn Gln Ser Ile Leu Gln Asn Ile Gly Ile
            385                 390                 395

aat cca gat agc cag cct gct aac cgg ata gtt gac cag gat gat tca    1251
Asn Pro Asp Ser Gln Pro Ala Asn Arg Ile Val Asp Gln Asp Asp Ser
            400                 405                 410

gtc caa agt cag gac caa aag acg caa gat gag cca gca gga gac caa    1299
Val Gln Ser Gln Asp Gln Lys Thr Gln Asp Glu Pro Ala Gly Asp Gln
        415                 420                 425

gct agt cag tcg gat agt cca gaa gaa ggc aat ttt aca gac aga atc    1347
Ala Ser Gln Ser Asp Ser Pro Glu Glu Gly Asn Phe Thr Asp Arg Ile
430                 435                 440                 445
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aag cat ttc ttt act aca ttt ttc gat taa
Lys His Phe Phe Thr Thr Phe Phe Asp
               450

                                                       1377

<210> 86
<211> 454
<212> PRT
<213> Alloiococcus otitidis

<400> 86
Met Phe Leu Asp Met Glu Val Ser Met Asn Met Lys Asn Gly Val Tyr
1   5   10   15

Thr Ser Leu Asp Ile Gly Thr Thr Ser Ile Lys Val Val Val Ser Glu
          20   25   30

Val Asp Asn Asn Gln Leu Lys Val Ile Gly Val Gly Lys Ala Gln Ser
       35   40   45

Lys Gly Leu Lys Arg Gly Met Val Val Asp Ile Asp Ala Thr Val Gln
    50   55   60

Ala Ile His Thr Ala Val Lys Gln Ala Ala Asp Lys Thr Gly Val Met
65   70   75   80

Ile Asn Gln Leu Ile Val Gly Val Pro Ala Asn Gly Val Ser Ile Glu
          85   90   95

Pro Cys His Gly Val Ile Thr Val Asp Asp Arg Ser Lys Glu Ile Asp
          100   105   110

Ser Gln Glu Val Asn Arg Val Val Asn Gln Ser Ile Ala Asn Ile Val
          115   120   125

Pro Pro Asp Arg Asp Leu Leu Ser Val Ser Leu Glu Glu Phe Ile Val
      130   135   140

Asp Gly Phe Asp Glu Ile His Asp Pro Arg Gly Met Val Gly Gln Arg
145   150   155   160

Leu Glu Leu Tyr Gly Thr Ala Ile Ser Val Pro Lys Thr Ile Leu His
             165   170   175

Asn Ile Arg Arg Cys Val Glu Lys Ala Gly Tyr Gln Ile Ala Ala Leu
          180   185   190

Ile Leu Gln Pro Gln Ala Met Ala Lys Val Ala Leu Ser Glu Asp Glu
195 200 205

Arg Asn Phe Gly Thr Val Met Val Asp Ile Gly Gly Gly Gln Thr Thr
210 215 220

Leu Ser Ala Ile His Asp Glu Gln Val Lys Tyr Ala Asn Val Val Gln
225 230 235 240

Glu Ala Gly Glu Tyr Ile Thr Lys Asp Ile Ser Ile Val Ile Asn Thr
245 250 255

Ser Gln Gln Asn Ala Glu Lys Leu Lys Arg Glu Val Gly Ala Ile Lys
260 265 270

Ser Gln Ser Asp Ser Thr Val Gln Val Asp Val Val Gly Gln Asn Glu
275 280 285

Pro Val Lys Ile Lys Glu Ser Tyr Val Gly Glu Ile Ile Glu Ala Arg
290 295 300

Val Ser Gln Ile Phe Glu Lys Val Lys Ala Asp Leu Asp Pro Ile Asn
305 310 315 320

Ala Phe Gln Leu Pro Gly Gly Ala Val Ile Ser Gly Gly Ser Ala Ala
325 330 335

Ile Pro Gly Ile Asp Ser Leu Ala Glu Asp Ile Phe Lys Val Arg Ser
340 345 350

Glu Leu Tyr Ile Pro Asp Tyr Met Gly Ile Arg Thr Pro Ala Phe Thr
355 360 365

Val Ala Val Gly Leu Thr Leu Tyr Gln Ala Gln Thr Ser Asp Ile Glu
370 375 380

Arg Ala Ile Asn Gln Ser Ile Leu Gln Asn Ile Gly Ile Asn Pro Asp
385 390 395 400

Ser Gln Pro Ala Asn Arg Ile Val Asp Gln Asp Asp Ser Val Gln Ser
405 410 415

Gln Asp Gln Lys Thr Gln Asp Glu Pro Ala Gly Asp Gln Ala Ser Gln
        420   425   430

Ser Asp Ser Pro Glu Glu Gly Asn Phe Thr Asp Arg Ile Lys His Phe
        435   440   445

Phe Thr Thr Phe Phe Asp
        450

<210> 87
<211> 1179
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (16)..(1179)
<223>

<400> 87
agcaaaggag caagt atg gaa act aaa aaa caa gca tta aaa gtt tta tta   51
              Met Glu Thr Lys Lys Gln Ala Leu Lys Val Leu Leu
               1   5   10

tca ggc ggt gga aca ggt ggc cat atc tac cca gcc ttg gcc ctt gct   99
Ser Gly Gly Gly Thr Gly Gly His Ile Tyr Pro Ala Leu Ala Leu Ala
        15   20   25

aag cac cta gct agc tta cac tca gat gtc gag ttt ttg tat gtt ggc   147
Lys His Leu Ala Ser Leu His Ser Asp Val Glu Phe Leu Tyr Val Gly
        30   35   40

act caa agg gga ttg gaa aat aaa ttg gtc ccc caa gca gga ctt gac   195
Thr Gln Arg Gly Leu Glu Asn Lys Leu Val Pro Gln Ala Gly Leu Asp
45   50   55   60

ttt atc ccg atc aaa gta gaa gga ttt agc cgg aag ttt aac ttc aaa   243
Phe Ile Pro Ile Lys Val Glu Gly Phe Ser Arg Lys Phe Asn Phe Lys
                   65   70   75

agc att aaa tat aat act aaa agt ctg att tat ttt cta aag gcc ctg   291
Ser Ile Lys Tyr Asn Thr Lys Ser Leu Ile Tyr Phe Leu Lys Ala Leu
        80   85   90

agt aag tct aag caa atc atc aaa gac ttt cag cca gat gtg gta ata   339
Ser Lys Ser Lys Gln Ile Ile Lys Asp Phe Gln Pro Asp Val Val Ile
        95   100   105

ggg aca ggt ggt tat gtt tgt gcc cct gtc ata tac cag gcg acc aag   387
Gly Thr Gly Gly Tyr Val Cys Ala Pro Val Ile Tyr Gln Ala Thr Lys
        110   115   120

tta ggc att cca agt ctc att cac gaa caa aat agt gtc gcc ggg gtg   435

```
        Leu Gly Ile Pro Ser Leu Ile His Glu Gln Asn Ser Val Ala Gly Val
        125             130             135             140

acc aat aag ttt ttg gct cgg tac gta gac aag att gcc cta agt ttc        483
Thr Asn Lys Phe Leu Ala Arg Tyr Val Asp Lys Ile Ala Leu Ser Phe
                145             150             155

cag gaa gct gaa aaa tcc ttt gcc aag tat aag gat aag ctg gtt ttg        531
Gln Glu Ala Glu Lys Ser Phe Ala Lys Tyr Lys Asp Lys Leu Val Leu
            160             165             170

act ggt aat cca aga gga cag gaa gtc agc caa gtc aag ggt ggc ctt        579
Thr Gly Asn Pro Arg Gly Gln Glu Val Ser Gln Val Lys Gly Gly Leu
            175             180             185

agc ctc cac aag tat ggc atg gac atg tcc caa cct tca gta att att        627
Ser Leu His Lys Tyr Gly Met Asp Met Ser Gln Pro Ser Val Ile Ile
            190             195             200

ttt ggt ggg tca agg ggg gct tat gct att aat aag gcc ttt gtt gag        675
Phe Gly Gly Ser Arg Gly Ala Tyr Ala Ile Asn Lys Ala Phe Val Glu
205             210             215             220

gca tat agt caa ctg gct gag agg gac tac cag gtc ttg ttt gtg ccg        723
Ala Tyr Ser Gln Leu Ala Glu Arg Asp Tyr Gln Val Leu Phe Val Pro
                225             230             235

gga tca gct aat ttt agc cgg ata aaa cag gaa att gat aac cgc tat        771
Gly Ser Ala Asn Phe Ser Arg Ile Lys Gln Glu Ile Asp Asn Arg Tyr
            240             245             250

ggc cag cat aag ccg tca aac att ttt att gaa tcc tat atc gat aac        819
Gly Gln His Lys Pro Ser Asn Ile Phe Ile Glu Ser Tyr Ile Asp Asn
            255             260             265

atg ccc caa gtt ttt aag gct att gac ttg gtg gtt tgc cgt agt ggg        867
Met Pro Gln Val Phe Lys Ala Ile Asp Leu Val Val Cys Arg Ser Gly
            270             275             280

gcc act acc cta gcc gaa att atg tca tta ggc ttg gcc agc att tta        915
Ala Thr Thr Leu Ala Glu Ile Met Ser Leu Gly Leu Ala Ser Ile Leu
285             290             295             300

att cca agt ccc aat gta acg gct gac cac caa acc aaa aat gct atg        963
Ile Pro Ser Pro Asn Val Thr Ala Asp His Gln Thr Lys Asn Ala Met
                305             310             315

agt ttg gtt aac caa caa gct ggc tta atg att aag gaa aat gat cta        1011
Ser Leu Val Asn Gln Gln Ala Gly Leu Met Ile Lys Glu Asn Asp Leu
                320             325             330

aat ggc caa agc ctc tta aac tgc tta gat gac ctg atg cat gat gac        1059
Asn Gly Gln Ser Leu Leu Asn Cys Leu Asp Asp Leu Met His Asp Asp
            335             340             345

gca aaa aga aac aag atg gcc caa caa gcg aaa gaa atg ggc caa ccc        1107
Ala Lys Arg Asn Lys Met Ala Gln Gln Ala Lys Glu Met Gly Gln Pro
```

```
        350                 355                 360
caa gct tca gac aag ttg atc gct ctc atc ttg tcc atg gtt aag gaa    1155
Gln Ala Ser Asp Lys Leu Ile Ala Leu Ile Leu Ser Met Val Lys Glu
365                 370                 375                 380
gat att aac tca gac atc gat taa                                    1179
Asp Ile Asn Ser Asp Ile Asp
                385
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<210> 88
<211> 387
<212> PRT
<213> Alloiococcus otitidis

<400> 88
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Met Glu Thr Lys Lys Gln Ala Leu Lys Val Leu Leu Ser Gly Gly Gly
1                 5                 10                15

Thr Gly Gly His Ile Tyr Pro Ala Leu Ala Leu Ala Lys His Leu Ala
        20                25                30

Ser Leu His Ser Asp Val Glu Phe Leu Tyr Val Gly Thr Gln Arg Gly
        35                40                45

Leu Glu Asn Lys Leu Val Pro Gln Ala Gly Leu Asp Phe Ile Pro Ile
    50                55                60

Lys Val Glu Gly Phe Ser Arg Lys Phe Asn Phe Lys Ser Ile Lys Tyr
65                70                75                80

Asn Thr Lys Ser Leu Ile Tyr Phe Leu Lys Ala Leu Ser Lys Ser Lys
                85                90                95

Gln Ile Ile Lys Asp Phe Gln Pro Asp Val Val Ile Gly Thr Gly Gly
            100                105                110

Tyr Val Cys Ala Pro Val Ile Tyr Gln Ala Thr Lys Leu Gly Ile Pro
        115                120                125

Ser Leu Ile His Glu Gln Asn Ser Val Ala Gly Val Thr Asn Lys Phe
        130                135                140

Leu Ala Arg Tyr Val Asp Lys Ile Ala Leu Ser Phe Gln Glu Ala Glu
145                150                155                160
```

Lys Ser Phe Ala Lys Tyr Lys Asp Lys Leu Val Leu Thr Gly Asn Pro
                165   170   175

Arg Gly Gln Glu Val Ser Gln Val Lys Gly Gly Leu Ser Leu His Lys
            180   185   190

Tyr Gly Met Asp Met Ser Gln Pro Ser Val Ile Ile Phe Gly Gly Ser
        195   200   205

Arg Gly Ala Tyr Ala Ile Asn Lys Ala Phe Val Glu Ala Tyr Ser Gln
    210   215   220

Leu Ala Glu Arg Asp Tyr Gln Val Leu Phe Val Pro Gly Ser Ala Asn
225   230   235   240

Phe Ser Arg Ile Lys Gln Glu Ile Asp Asn Arg Tyr Gly Gln His Lys
                245   250   255

Pro Ser Asn Ile Phe Ile Glu Ser Tyr Ile Asp Asn Met Pro Gln Val
                260   265   270

Phe Lys Ala Ile Asp Leu Val Val Cys Arg Ser Gly Ala Thr Thr Leu
                275   280   285

Ala Glu Ile Met Ser Leu Gly Leu Ala Ser Ile Leu Ile Pro Ser Pro
    290   295   300

Asn Val Thr Ala Asp His Gln Thr Lys Asn Ala Met Ser Leu Val Asn
305   310   315   320

Gln Gln Ala Gly Leu Met Ile Lys Glu Asn Asp Leu Asn Gly Gln Ser
                325   330   335

Leu Leu Asn Cys Leu Asp Asp Leu Met His Asp Asp Ala Lys Arg Asn
                340   345   350

Lys Met Ala Gln Gln Ala Lys Glu Met Gly Gln Pro Gln Ala Ser Asp
        355   360   365

Lys Leu Ile Ala Leu Ile Leu Ser Met Val Lys Glu Asp Ile Asn Ser
    370   375   380

Asp Ile Asp

385

<210> 89
<211> 1428
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (25)..(1428)
<223>

<400> 89
cgttacttag aaaggtttgg caag atg gtt gat tcg gta ttt tgc aat aag   51
                          Met Val Asp Ser Val Phe Cys Asn Lys
                          1   5

aag gtt tta gtt tta ggc ttg gca aaa agc ggg ctc agt gcg gcc cat   99
Lys Val Leu Val Leu Gly Leu Ala Lys Ser Gly Leu Ser Ala Ala His
10   15   20   25

ttg tta aaa aaa cta ggg gcc aag gtc atc gtc aat gac aag ttg gcc   147
Leu Leu Lys Lys Leu Gly Ala Lys Val Ile Val Asn Asp Lys Leu Ala
                30   35   40

cta gaa aat aat acg gaa gcc cag gtc tta att gaa gag ggc ttc caa   195
Leu Glu Asn Asn Thr Glu Ala Gln Val Leu Ile Glu Glu Gly Phe Gln
            45   50   55

gtt atc acc ggc tac cac cca gag gat tta ctt gat gca agc ttt gac   243
Val Ile Thr Gly Tyr His Pro Glu Asp Leu Leu Asp Ala Ser Phe Asp
            60   65   70

ttt gtc gtc aag aat ccg ggc att cct tac acc aat cca gtg gta ggc   291
Phe Val Val Lys Asn Pro Gly Ile Pro Tyr Thr Asn Pro Val Val Gly
        75   80   85

cag gct gaa aaa ctg gct att ccc att tta act gaa gtg gac gtg gca   339
Gln Ala Glu Lys Leu Ala Ile Pro Ile Leu Thr Glu Val Asp Val Ala
90   95   100   105

gga agc atc tta aaa gcc aag ccc atc gct gtt acc ggg acc aat ggc   387
Gly Ser Ile Leu Lys Ala Lys Pro Ile Ala Val Thr Gly Thr Asn Gly
                110   115   120

aag aca act acc gta tct tta att tat gat att tta gcc caa gat caa   435
Lys Thr Thr Thr Val Ser Leu Ile Tyr Asp Ile Leu Ala Gln Asp Gln
                125   130   135

gcg gaa agc cct gaa cct aaa cca gtc tac aag cta ggc aat att ggc   483
Ala Glu Ser Pro Glu Pro Lys Pro Val Tyr Lys Leu Gly Asn Ile Gly
            140   145   150

caa ccg gtt agt gac ttg gcc tta gaa att aaa gct gaa tct aac ctg   531
Gln Pro Val Ser Asp Leu Ala Leu Glu Ile Lys Ala Glu Ser Asn Leu
            155   160   165

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gtt gtc gaa ctc tct agt ttc caa cta cag tca ctg acc tat ttc acc    579
Val Val Glu Leu Ser Ser Phe Gln Leu Gln Ser Leu Thr Tyr Phe Thr
170             175             180             185

cct cat ata gca gtc att acc aat att tat tcc gcc cac ctt gac tac    627
Pro His Ile Ala Val Ile Thr Asn Ile Tyr Ser Ala His Leu Asp Tyr
            190             195             200

cat aag agt cgg gag gaa tat gtt agg gct aag cta agg att acc cag    675
His Lys Ser Arg Glu Glu Tyr Val Arg Ala Lys Leu Arg Ile Thr Gln
            205             210             215

gct caa ggt ccg gat gac tac cta gtc tac tac cag ggt cag gaa gaa    723
Ala Gln Gly Pro Asp Asp Tyr Leu Val Tyr Tyr Gln Gly Gln Glu Glu
            220             225             230

ttg gct agc ctg gtc aaa aaa tac tct aaa gcc cag ctg gtc ccc tat    771
Leu Ala Ser Leu Val Lys Lys Tyr Ser Lys Ala Gln Leu Val Pro Tyr
        235             240             245

act gac aag ggt caa ctg aac caa gga gcc tat atc aag gat gac tat    819
Thr Asp Lys Gly Gln Leu Asn Gln Gly Ala Tyr Ile Lys Asp Asp Tyr
250             255             260             265

ctt atc tat aat caa gag cca gtc atg gct tta gac cga gtt caa gtt    867
Leu Ile Tyr Asn Gln Glu Pro Val Met Ala Leu Asp Arg Val Gln Val
                270             275             280

tct ggt agc cac aac tta caa aat att tta gca gct gtt tgc gta gct    915
Ser Gly Ser His Asn Leu Gln Asn Ile Leu Ala Ala Val Cys Val Ala
            285             290             295

aaa ata aag ggg ctc tct aac caa acc att gcc caa gct gtc aac cac    963
Lys Ile Lys Gly Leu Ser Asn Gln Thr Ile Ala Gln Ala Val Asn His
        300             305             310

ttc aaa ggg gtt gcc cac cgc agc cag gtg gtt ggg cgg tat gag gac   1011
Phe Lys Gly Val Ala His Arg Ser Gln Val Val Gly Arg Tyr Glu Asp
    315             320             325

cgg ctt ttt gtc aac gac tct aag gca acc aat agc ttg gcc aca cag   1059
Arg Leu Phe Val Asn Asp Ser Lys Ala Thr Asn Ser Leu Ala Thr Gln
330             335             340             345

aag gca tta gaa gcc tat gac caa gat acc atc ttg tta gtg ggt ggc   1107
Lys Ala Leu Glu Ala Tyr Asp Gln Asp Thr Ile Leu Leu Val Gly Gly
            350             355             360

cta gac cgc caa gat gat ttt tcc aag ctt gac cat gct cta aac agg   1155
Leu Asp Arg Gln Asp Asp Phe Ser Lys Leu Asp His Ala Leu Asn Arg
            365             370             375

gtt aag ggg gtc gtt tgt ttt ggc cag acc aaa gat aag tta gcc cgg   1203
Val Lys Gly Val Val Cys Phe Gly Gln Thr Lys Asp Lys Leu Ala Arg
        380             385             390
```

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tat ttt aaa gac cgt cac att gag ggt gtt gag ctt gcc cag aca gtt      1251
Tyr Phe Lys Asp Arg His Ile Glu Gly Val Glu Leu Ala Gln Thr Val
    395             400                 405

cct gaa gca gtt gat ttg gct tac gac ttg agt gag cca gga caa gtc      1299
Pro Glu Ala Val Asp Leu Ala Tyr Asp Leu Ser Glu Pro Gly Gln Val
410             415                 420                 425

att tta ttt tct cct gct tgt gca agt tgg gac caa tat gct aac ttt      1347
Ile Leu Phe Ser Pro Ala Cys Ala Ser Trp Asp Gln Tyr Ala Asn Phe
                430                 435                 440

gaa gag aga gga caa gat tat gtt gat gca atc cag cag ctg gtt gaa      1395
Glu Glu Arg Gly Gln Asp Tyr Val Asp Ala Ile Gln Gln Leu Val Glu
            445                 450                 455

aga cta gag caa agg agc aag tat gga aac taa                          1428
Arg Leu Glu Gln Arg Ser Lys Tyr Gly Asn
            460                 465
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<210> 90
<211> 467
<212> PRT
<213> Alloiococcus otitidis
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<400> 90
Met Val Asp Ser Val Phe Cys Asn Lys Lys Val Leu Val Leu Gly Leu
1               5               10                  15


Ala Lys Ser Gly Leu Ser Ala Ala His Leu Leu Lys Lys Leu Gly Ala
            20                  25                  30


Lys Val Ile Val Asn Asp Lys Leu Ala Leu Glu Asn Asn Thr Glu Ala
            35                  40                  45


Gln Val Leu Ile Glu Glu Gly Phe Gln Val Ile Thr Gly Tyr His Pro
    50                  55                  60


Glu Asp Leu Leu Asp Ala Ser Phe Asp Phe Val Val Lys Asn Pro Gly
65                  70                  75                  80


Ile Pro Tyr Thr Asn Pro Val Val Gly Gln Ala Glu Lys Leu Ala Ile
                85                  90                  95


Pro Ile Leu Thr Glu Val Asp Val Ala Gly Ser Ile Leu Lys Ala Lys
                100                 105                 110


Pro Ile Ala Val Thr Gly Thr Asn Gly Lys Thr Thr Thr Val Ser Leu
                115                 120                 125
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Ile Tyr Asp Ile Leu Ala Gln Asp Gln Ala Glu Ser Pro Glu Pro Lys
130   135   140

Pro Val Tyr Lys Leu Gly Asn Ile Gly Gln Pro Val Ser Asp Leu Ala
145   150   155   160

Leu Glu Ile Lys Ala Glu Ser Asn Leu Val Val Glu Leu Ser Ser Phe
              165   170   175

Gln Leu Gln Ser Leu Thr Tyr Phe Thr Pro His Ile Ala Val Ile Thr
              180   185   190

Asn Ile Tyr Ser Ala His Leu Asp Tyr His Lys Ser Arg Glu Glu Tyr
              195   200   205

Val Arg Ala Lys Leu Arg Ile Thr Gln Ala Gln Gly Pro Asp Asp Tyr
    210   215   220

Leu Val Tyr Tyr Gln Gly Gln Glu Glu Leu Ala Ser Leu Val Lys Lys
225   230   235   240

Tyr Ser Lys Ala Gln Leu Val Pro Tyr Thr Asp Lys Gly Gln Leu Asn
              245   250   255

Gln Gly Ala Tyr Ile Lys Asp Asp Tyr Leu Ile Tyr Asn Gln Glu Pro
              260   265   270

Val Met Ala Leu Asp Arg Val Gln Val Ser Gly Ser His Asn Leu Gln
    275   280   285

Asn Ile Leu Ala Ala Val Cys Val Ala Lys Ile Lys Gly Leu Ser Asn
    290   295   300

Gln Thr Ile Ala Gln Ala Val Asn His Phe Lys Gly Val Ala His Arg
305   310   315   320

Ser Gln Val Val Gly Arg Tyr Glu Asp Arg Leu Phe Val Asn Asp Ser
              325   330   335

Lys Ala Thr Asn Ser Leu Ala Thr Gln Lys Ala Leu Glu Ala Tyr Asp
              340   345   350

Gln Asp Thr Ile Leu Leu Val Gly Gly Leu Asp Arg Gln Asp Asp Phe
    355   360   365

Ser Lys Leu Asp His Ala Leu Asn Arg Val Lys Gly Val Val Cys Phe
    370   375   380

Gly Gln Thr Lys Asp Lys Leu Ala Arg Tyr Phe Lys Asp Arg His Ile
385   390   395   400

Glu Gly Val Glu Leu Ala Gln Thr Val Pro Glu Ala Val Asp Leu Ala
            405   410   415

Tyr Asp Leu Ser Glu Pro Gly Gln Val Ile Leu Phe Ser Pro Ala Cys
        420   425   430

Ala Ser Trp Asp Gln Tyr Ala Asn Phe Glu Glu Arg Gly Gln Asp Tyr
    435   440   445

Val Asp Ala Ile Gln Gln Leu Val Glu Arg Leu Glu Gln Arg Ser Lys
    450   455   460

Tyr Gly Asn
465

<210> 91
<211> 651
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (7)..(651)
<223>

<400> 91
actagt atg aag caa aaa act caa gcg aca gcg gtc aac cag acc caa   48
       Met Lys Gln Lys Thr Gln Ala Thr Ala Val Asn Gln Thr Gln
        1   5   10

aca gag gca gaa gaa aga caa gaa acc cgt cgg aaa att ggc ctc atg   96
Thr Glu Ala Glu Glu Arg Gln Glu Thr Arg Arg Lys Ile Gly Leu Met
15   20   25   30

ggg ggg acc ttt aat ccg ccc cat ctg ggt cat tta ctg gta gct gaa   144
Gly Gly Thr Phe Asn Pro Pro His Leu Gly His Leu Leu Val Ala Glu
                35   40   45

caa gtt tat gag gcc ttg gac ttg gat aat att cac ttt atg ccc act   192

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Gln Val Tyr Glu Ala Leu Asp Leu Asp Asn Ile His Phe Met Pro Thr
        50                  55                  60

gca aag ccg ggc cat gcc gct ggt aag gaa acc ata gat gcc tct tac      240
Ala Lys Pro Gly His Ala Ala Gly Lys Glu Thr Ile Asp Ala Ser Tyr
        65                  70                  75

cgg gtt gat atg gtg gat tat gcc atc gaa gat aac ccc cac ttt tct      288
Arg Val Asp Met Val Asp Tyr Ala Ile Glu Asp Asn Pro His Phe Ser
        80                  85                  90

ctt aac ttg act gaa gtg aac cgg gga ggg aca act tac acc atc gat      336
Leu Asn Leu Thr Glu Val Asn Arg Gly Gly Thr Thr Tyr Thr Ile Asp
95                  100                 105                 110

acc att aaa gaa ttg aaa gag gct agc ccg aat aca gat tat tac ttc      384
Thr Ile Lys Glu Leu Lys Glu Ala Ser Pro Asn Thr Asp Tyr Tyr Phe
                115                 120                 125

att att ggt gag gat tca gtt atg gat ttg gcc cag tgg aag aat att      432
Ile Ile Gly Glu Asp Ser Val Met Asp Leu Ala Gln Trp Lys Asn Ile
        130                 135                 140

gaa caa tta ctg gat tta gtt caa ttt gtt ggt gtg aag cga cca ggc      480
Glu Gln Leu Leu Asp Leu Val Gln Phe Val Gly Val Lys Arg Pro Gly
        145                 150                 155

tac caa gct gat gtg gac ttt ccc att att tgg gtg gat acg cca gaa      528
Tyr Gln Ala Asp Val Asp Phe Pro Ile Ile Trp Val Asp Thr Pro Glu
        160                 165                 170

cta gat att agt tca agt gac atc agg caa agg gtg gca gaa ggg caa      576
Leu Asp Ile Ser Ser Ser Asp Ile Arg Gln Arg Val Ala Glu Gly Gln
175                 180                 185                 190

tcc att aaa tat ttg acc cca gat agg gta aga gat tat att gaa gac      624
Ser Ile Lys Tyr Leu Thr Pro Asp Arg Val Arg Asp Tyr Ile Glu Asp
                195                 200                 205

aat ggc tta tat aag ggt gaa gaa taa                                  651
Asn Gly Leu Tyr Lys Gly Glu Glu
        210


<210> 92
<211> 214
<212> PRT
<213> Alloiococcus otitidis

<400> 92
Met Lys Gln Lys Thr Gln Ala Thr Ala Val Asn Gln Thr Gln Thr Glu
1               5                   10                  15


Ala Glu Glu Arg Gln Glu Thr Arg Arg Lys Ile Gly Leu Met Gly Gly
        20                  25                  30
```

Thr Phe Asn Pro Pro His Leu Gly His Leu Leu Val Ala Glu Gln Val
        35   40   45

Tyr Glu Ala Leu Asp Leu Asp Asn Ile His Phe Met Pro Thr Ala Lys
    50   55   60

Pro Gly His Ala Ala Gly Lys Glu Thr Ile Asp Ala Ser Tyr Arg Val
65   70   75   80

Asp Met Val Asp Tyr Ala Ile Glu Asp Asn Pro His Phe Ser Leu Asn
            85   90   95

Leu Thr Glu Val Asn Arg Gly Gly Thr Thr Tyr Thr Ile Asp Thr Ile
        100   105   110

Lys Glu Leu Lys Glu Ala Ser Pro Asn Thr Asp Tyr Tyr Phe Ile Ile
        115   120   125

Gly Glu Asp Ser Val Met Asp Leu Ala Gln Trp Lys Asn Ile Glu Gln
    130   135   140

Leu Leu Asp Leu Val Gln Phe Val Gly Val Lys Arg Pro Gly Tyr Gln
145   150   155   160

Ala Asp Val Asp Phe Pro Ile Ile Trp Val Asp Thr Pro Glu Leu Asp
            165   170   175

Ile Ser Ser Ser Asp Ile Arg Gln Arg Val Ala Glu Gly Gln Ser Ile
        180   185   190

Lys Tyr Leu Thr Pro Asp Arg Val Arg Asp Tyr Ile Glu Asp Asn Gly
    195   200   205

Leu Tyr Lys Gly Glu Glu
    210

<210> 93
<211> 666
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (1)..(666)

<223>

<400> 93
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atg gta ggg gga ctc att ttt gtc ctc act gcc agc aat aaa agg aaa    48
Met Val Gly Gly Leu Ile Phe Val Leu Thr Ala Ser Asn Lys Arg Lys
1               5                  10                  15

gga agt ttg tcc atg acc tat ttg tta ggc cta acc ggt ggc att gcc    96
Gly Ser Leu Ser Met Thr Tyr Leu Leu Gly Leu Thr Gly Gly Ile Ala
                20                  25                  30

agt ggg aag tct act gtt agc cag gtt ttt aag gaa aag ggt atc caa   144
Ser Gly Lys Ser Thr Val Ser Gln Val Phe Lys Glu Lys Gly Ile Gln
        35                  40                  45

gtg gtt gat gct gac cga gtt gcc cga cag gtt gtt gaa cct gga agt   192
Val Val Asp Ala Asp Arg Val Ala Arg Gln Val Val Glu Pro Gly Ser
    50                  55                  60

cca ggc tta gac cag ctt gtt gat tat ttt ggc cag gag att ttg acc   240
Pro Gly Leu Asp Gln Leu Val Asp Tyr Phe Gly Gln Glu Ile Leu Thr
65                  70                  75                  80

cag gat ggg ggc ttg gac cgc aaa tat tta ggc gac ctt atc ttc cgg   288
Gln Asp Gly Gly Leu Asp Arg Lys Tyr Leu Gly Asp Leu Ile Phe Arg
                85                  90                  95

aat agc cag gcc aag gag gct gtc aac cgg atc ctc cac cct ttg att   336
Asn Ser Gln Ala Lys Glu Ala Val Asn Arg Ile Leu His Pro Leu Ile
                100                 105                 110

agg cag tct atc caa aat caa att aaa act gcc ata ggc caa gac ttg   384
Arg Gln Ser Ile Gln Asn Gln Ile Lys Thr Ala Ile Gly Gln Asp Leu
            115                 120                 125

gat ttg tta gtt tta gac atc ccc ctc ctt tac gag aca ggt cag gca   432
Asp Leu Leu Val Leu Asp Ile Pro Leu Leu Tyr Glu Thr Gly Gln Ala
        130                 135                 140

gac gac tac cag gcc gtc atg gtg gtt tcg ctt ccc tac cag gac cag   480
Asp Asp Tyr Gln Ala Val Met Val Val Ser Leu Pro Tyr Gln Asp Gln
145                 150                 155                 160

gtg agt cgg tta atg gac cgg gat ggg att gac cga gac caa gcc ctg   528
Val Ser Arg Leu Met Asp Arg Asp Gly Ile Asp Arg Asp Gln Ala Leu
                165                 170                 175

cgc aag att cag gcc caa atg tca ttg gaa gaa aaa gtg aag ttg gcg   576
Arg Lys Ile Gln Ala Gln Met Ser Leu Glu Glu Lys Val Lys Leu Ala
            180                 185                 190

gac tat gtc att gat aac agc gga agc aag gaa gaa agc cgt cag cag   624
Asp Tyr Val Ile Asp Asn Ser Gly Ser Lys Glu Glu Ser Arg Gln Gln
        195                 200                 205

gtt gaa gct tgg ttg gat caa aag ggt ttt aaa aac ttg taa          666
Val Glu Ala Trp Leu Asp Gln Lys Gly Phe Lys Asn Leu
```

210   215   220

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<210> 94
<211> 221
<212> PRT
<213> Alloiococcus otitidis

<400> 94
Met Val Gly Gly Leu Ile Phe Val Leu Thr Ala Ser Asn Lys Arg Lys
1               5                   10                  15


Gly Ser Leu Ser Met Thr Tyr Leu Leu Gly Leu Thr Gly Gly Ile Ala
            20                  25                  30


Ser Gly Lys Ser Thr Val Ser Gln Val Phe Lys Glu Lys Gly Ile Gln
        35                  40                  45


Val Val Asp Ala Asp Arg Val Ala Arg Gln Val Val Glu Pro Gly Ser
    50                  55                  60


Pro Gly Leu Asp Gln Leu Val Asp Tyr Phe Gly Gln Glu Ile Leu Thr
65                  70                  75                  80


Gln Asp Gly Gly Leu Asp Arg Lys Tyr Leu Gly Asp Leu Ile Phe Arg
                85                  90                  95


Asn Ser Gln Ala Lys Glu Ala Val Asn Arg Ile Leu His Pro Leu Ile
            100                 105                 110


Arg Gln Ser Ile Gln Asn Gln Ile Lys Thr Ala Ile Gly Gln Asp Leu
        115                 120                 125


Asp Leu Leu Val Leu Asp Ile Pro Leu Leu Tyr Glu Thr Gly Gln Ala
    130                 135                 140


Asp Asp Tyr Gln Ala Val Met Val Val Ser Leu Pro Tyr Gln Asp Gln
145                 150                 155                 160


Val Ser Arg Leu Met Asp Arg Asp Gly Ile Asp Arg Asp Gln Ala Leu
            165                 170                 175


Arg Lys Ile Gln Ala Gln Met Ser Leu Glu Glu Lys Val Lys Leu Ala
            180                 185                 190
```

```
Asp Tyr Val Ile Asp Asn Ser Gly Ser Lys Glu Glu Ser Arg Gln Gln
        195                 200                 205


Val Glu Ala Trp Leu Asp Gln Lys Gly Phe Lys Asn Leu
        210                 215                 220
```

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<210> 95
<211> 1335
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (4)..(1335)
<223>

<400> 95
ggt atg gac caa gac acc atc tat cac ttt gtt ggc att aaa gga tct      48
    Met Asp Gln Asp Thr Ile Tyr His Phe Val Gly Ile Lys Gly Ser
    1               5                   10                  15

ggc atg agt tca ctt gcc act atc ttg ttt gac aag ggc tta aat gtc      96
Gly Met Ser Ser Leu Ala Thr Ile Leu Phe Asp Lys Gly Leu Asn Val
                20                  25                  30

caa gga tct gat gtc aaa aag tat ttc ttt acc caa aaa agc tta gaa     144
Gln Gly Ser Asp Val Lys Lys Tyr Phe Phe Thr Gln Lys Ser Leu Glu
            35                  40                  45

gaa aaa aat ata aac att tta gaa ttt gac cct gat aac atc aaa cca     192
Glu Lys Asn Ile Asn Ile Leu Glu Phe Asp Pro Asp Asn Ile Lys Pro
        50                  55                  60

ggt atg acc ctg ata gca ggc aat gcc ttt gga gac aac cat ccc gag     240
Gly Met Thr Leu Ile Ala Gly Asn Ala Phe Gly Asp Asn His Pro Glu
    65                  70                  75

ctg gtc cga ggt cga gag ctc ggt tta gaa atc atc cgc tac cat gat     288
Leu Val Arg Gly Arg Glu Leu Gly Leu Glu Ile Ile Arg Tyr His Asp
80                  85                  90                  95

ttt atc ggt gac ctt atc gaa cac ttt act tcc atc gct att acc ggg     336
Phe Ile Gly Asp Leu Ile Glu His Phe Thr Ser Ile Ala Ile Thr Gly
                100                 105                 110

tct cac ggt aag acc tcc aca act ggt ttg atg gcc cat gtt ttc tcc     384
Ser His Gly Lys Thr Ser Thr Thr Gly Leu Met Ala His Val Phe Ser
            115                 120                 125

ggt att gat agc acc tcc tac tta att gga gat ggg acc ggc cat ggg     432
Gly Ile Asp Ser Thr Ser Tyr Leu Ile Gly Asp Gly Thr Gly His Gly
        130                 135                 140

gaa aaa ggt gcc aag tat ttt gtc ttg gaa gcc tgc gaa tac aag cgg     480
Glu Lys Gly Ala Lys Tyr Phe Val Leu Glu Ala Cys Glu Tyr Lys Arg
```

```
                 145                        150                            155

     cac ttt ttg gcc tac cga ccg gac tat gcg gtt atg acc aat att gac          528
     His Phe Leu Ala Tyr Arg Pro Asp Tyr Ala Val Met Thr Asn Ile Asp
     160                     165                 170                 175

     ttt gac cac ccg gac tat tac aag tct att gaa gat gtc caa gtg gcc          576
     Phe Asp His Pro Asp Tyr Tyr Lys Ser Ile Glu Asp Val Gln Val Ala
                         180                 185                 190

     ttt gat gaa ttc agc cac cag gtc aaa aaa tac ctc ttt gcc tgc ggg          624
     Phe Asp Glu Phe Ser His Gln Val Lys Lys Tyr Leu Phe Ala Cys Gly
                     195                 200                 205

     gac gac caa cgt ctt cgg cag gtc aaa gcc cag gtg ccg gtc att tac          672
     Asp Asp Gln Arg Leu Arg Gln Val Lys Ala Gln Val Pro Val Ile Tyr
                 210                 215                 220

     tac ggt cta aat gaa gac aat gac ttt gtg gct aaa aac atc gac cga          720
     Tyr Gly Leu Asn Glu Asp Asn Asp Phe Val Ala Lys Asn Ile Asp Arg
                 225                 230                 235

     agt cgt gaa ggg tct gcc ttc gac ctt tat att aag gga gaa ttt tac          768
     Ser Arg Glu Gly Ser Ala Phe Asp Leu Tyr Ile Lys Gly Glu Phe Tyr
     240                     245                 250                 255

     aaa cac ttc acc atc cca acc tat ggc aac cac aat att caa aat gcc          816
     Lys His Phe Thr Ile Pro Thr Tyr Gly Asn His Asn Ile Gln Asn Ala
                         260                 265                 270

     ttg gcg gtt ata gca gta gct tac tac gaa ggg tta gac caa gat ttg          864
     Leu Ala Val Ile Ala Val Ala Tyr Tyr Glu Gly Leu Asp Gln Asp Leu
                     275                 280                 285

     gtt gcc caa aga ttg gct aat ttt gct ggg gtg aaa cgc cgg ttt acc          912
     Val Ala Gln Arg Leu Ala Asn Phe Ala Gly Val Lys Arg Arg Phe Thr
                 290                 295                 300

     gag aag gtg gtc ggg gac act act att atc gat gac tat gct cac cac          960
     Glu Lys Val Val Gly Asp Thr Thr Ile Ile Asp Asp Tyr Ala His His
     305                     310                 315

     cct gct gaa ata agg gca acg att gat gcg gcc cgg caa aaa tac ccg         1008
     Pro Ala Glu Ile Arg Ala Thr Ile Asp Ala Ala Arg Gln Lys Tyr Pro
     320                     325                 330                 335

     gac aag gac att gtg acg gtc ttc cag ccc cac acc ttt acc cgg aca         1056
     Asp Lys Asp Ile Val Thr Val Phe Gln Pro His Thr Phe Thr Arg Thr
                         340                 345                 350

     gtc gcc ctc cta gat gaa ttt gcc cag gcc ttg gac ttg gca gac cag         1104
     Val Ala Leu Leu Asp Glu Phe Ala Gln Ala Leu Asp Leu Ala Asp Gln
                     355                 360                 365

     gtt tac ttg tgt gat atc ttt aat tca gct aga gaa aag tca ggc gat         1152
     Val Tyr Leu Cys Asp Ile Phe Asn Ser Ala Arg Glu Lys Ser Gly Asp
                 370                 375                 380
```

```
att tcc atc caa gat ctt ttg gct aaa acc agc aag gcc gac cag gtg          1200
Ile Ser Ile Gln Asp Leu Leu Ala Lys Thr Ser Lys Ala Asp Gln Val
    385             390             395

att gag gaa gac gat gtg tct cct ctg ctt gac caa cat ggg caa gtg          1248
Ile Glu Glu Asp Asp Val Ser Pro Leu Leu Asp Gln His Gly Gln Val
400             405             410             415

att att ttc atg gga gca gga gac atc agc aag ttt gaa aaa gcc tat          1296
Ile Ile Phe Met Gly Ala Gly Asp Ile Ser Lys Phe Glu Lys Ala Tyr
                420             425             430

gaa agc ttg ttg agc tca acc tac cac tcc cag gtc taa                      1335
Glu Ser Leu Leu Ser Ser Thr Tyr His Ser Gln Val
            435             440
```

```
<210> 96
<211> 443
<212> PRT
<213> Alloiococcus otitidis

<400> 96
Met Asp Gln Asp Thr Ile Tyr His Phe Val Gly Ile Lys Gly Ser Gly
1               5                   10                  15


Met Ser Ser Leu Ala Thr Ile Leu Phe Asp Lys Gly Leu Asn Val Gln
            20              25              30


Gly Ser Asp Val Lys Lys Tyr Phe Phe Thr Gln Lys Ser Leu Glu Glu
        35              40              45


Lys Asn Ile Asn Ile Leu Glu Phe Asp Pro Asp Asn Ile Lys Pro Gly
    50              55              60


Met Thr Leu Ile Ala Gly Asn Ala Phe Gly Asp Asn His Pro Glu Leu
65              70              75              80


Val Arg Gly Arg Glu Leu Gly Leu Glu Ile Ile Arg Tyr His Asp Phe
                85              90              95


Ile Gly Asp Leu Ile Glu His Phe Thr Ser Ile Ala Ile Thr Gly Ser
            100             105             110


His Gly Lys Thr Ser Thr Thr Gly Leu Met Ala His Val Phe Ser Gly
        115             120             125


Ile Asp Ser Thr Ser Tyr Leu Ile Gly Asp Gly Thr Gly His Gly Glu
```

                    130   135   140

Lys Gly Ala Lys Tyr Phe Val Leu Glu Ala Cys Glu Tyr Lys Arg His
145   150   155   160

Phe Leu Ala Tyr Arg Pro Asp Tyr Ala Val Met Thr Asn Ile Asp Phe
                 165   170   175

Asp His Pro Asp Tyr Tyr Lys Ser Ile Glu Asp Val Gln Val Ala Phe
                 180   185   190

Asp Glu Phe Ser His Gln Val Lys Lys Tyr Leu Phe Ala Cys Gly Asp
                 195   200   205

Asp Gln Arg Leu Arg Gln Val Lys Ala Gln Val Pro Val Ile Tyr Tyr
     210   215   220

Gly Leu Asn Glu Asp Asn Asp Phe Val Ala Lys Asn Ile Asp Arg Ser
225   230   235   240

Arg Glu Gly Ser Ala Phe Asp Leu Tyr Ile Lys Gly Glu Phe Tyr Lys
                 245   250   255

His Phe Thr Ile Pro Thr Tyr Gly Asn His Asn Ile Gln Asn Ala Leu
                 260   265   270

Ala Val Ile Ala Val Ala Tyr Tyr Glu Gly Leu Asp Gln Asp Leu Val
                 275   280   285

Ala Gln Arg Leu Ala Asn Phe Ala Gly Val Lys Arg Arg Phe Thr Glu
     290   295   300

Lys Val Val Gly Asp Thr Thr Ile Ile Asp Asp Tyr Ala His His Pro
305   310   315   320

Ala Glu Ile Arg Ala Thr Ile Asp Ala Ala Arg Gln Lys Tyr Pro Asp
                 325   330   335

Lys Asp Ile Val Thr Val Phe Gln Pro His Thr Phe Thr Arg Thr Val
                 340   345   350

Ala Leu Leu Asp Glu Phe Ala Gln Ala Leu Asp Leu Ala Asp Gln Val
                 355   360   365

```
Tyr Leu Cys Asp Ile Phe Asn Ser Ala Arg Glu Lys Ser Gly Asp Ile
    370                 375                 380

Ser Ile Gln Asp Leu Leu Ala Lys Thr Ser Lys Ala Asp Gln Val Ile
385                 390                 395                 400

Glu Glu Asp Asp Val Ser Pro Leu Leu Asp Gln His Gly Gln Val Ile
                405                 410                 415

Ile Phe Met Gly Ala Gly Asp Ile Ser Lys Phe Glu Lys Ala Tyr Glu
                420                 425                 430

Ser Leu Leu Ser Ser Thr Tyr His Ser Gln Val
        435                 440
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<210> 97
<211> 1050
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (19)..(1050)
<223>

<400> 97

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acaaaattat ttacgtgt atg gag gaa tta ata gtg cca tta tta gac tta          51
                    Met Glu Glu Leu Ile Val Pro Leu Leu Asp Leu
                     1               5                   10

aat gac cat gac cgc gtt cag gaa tat gag gac ttt gtc caa aac cac          99
Asn Asp His Asp Arg Val Gln Glu Tyr Glu Asp Phe Val Gln Asn His
                15                   20                   25

ccc cag ggc cac ctg atg cag tct acc aaa tgg atc cag gtt aag gaa          147
Pro Gln Gly His Leu Met Gln Ser Thr Lys Trp Ile Gln Val Lys Glu
            30                   35                   40

ggc tgg gac ggt gac tat gtt tac ctt acc gat gac caa gac cgg atc          195
Gly Trp Asp Gly Asp Tyr Val Tyr Leu Thr Asp Asp Gln Asp Arg Ile
    45                   50                   55

aag gca tgc ttg tcc att cta tca gtc aaa aat gac gga gaa cat gcc          243
Lys Ala Cys Leu Ser Ile Leu Ser Val Lys Asn Asp Gly Glu His Ala
60                   65                   70                   75

ttc tta tat gcg cca aga ggg ccg gtt tgt gac ttt cat gat aca gac          291
Phe Leu Tyr Ala Pro Arg Gly Pro Val Cys Asp Phe His Asp Thr Asp
                80                   85                   90
```

```
ttg gtg acc gac tta att aag gaa gcc caa gtc gta gcg gac aag cac     339
Leu Val Thr Asp Leu Ile Lys Glu Ala Gln Val Val Ala Asp Lys His
         95              100             105

aag gcc ttt ttg ttg cgg atg gac ccg gaa acc ctt cat gat cct gac     387
Lys Ala Phe Leu Leu Arg Met Asp Pro Glu Thr Leu His Asp Pro Asp
        110             115             120

ctg gtc gaa aaa tac cgc gat tta ggc tat act ttc cgg tca gct gag     435
Leu Val Glu Lys Tyr Arg Asp Leu Gly Tyr Thr Phe Arg Ser Ala Glu
        125             130             135

caa gaa gat gaa cac gtc ttc tcc aac ccc cgc ttc cac atg atg acg     483
Gln Glu Asp Glu His Val Phe Ser Asn Pro Arg Phe His Met Met Thr
140             145             150             155

gac tta agg ggt cat gat gaa gaa agc ttg ctg atg gcc ttc acc agc     531
Asp Leu Arg Gly His Asp Glu Glu Ser Leu Leu Met Ala Phe Thr Ser
            160             165             170

aat aac cgg cgc aag atc cgc aaa act tac aaa aat aac ctc cag acc     579
Asn Asn Arg Arg Lys Ile Arg Lys Thr Tyr Lys Asn Asn Leu Gln Thr
        175             180             185

cac tat ctg acc gtg gat gat gag ggt tat gac cag gcc ttg gat gac     627
His Tyr Leu Thr Val Asp Asp Glu Gly Tyr Asp Gln Ala Leu Asp Asp
        190             195             200

ttt tat gaa ttg acc caa ata atg gca gaa cgg caa ggg att act cac     675
Phe Tyr Glu Leu Thr Gln Ile Met Ala Glu Arg Gln Gly Ile Thr His
        205             210             215

cgg ccc aaa gac tac ttt gac cgg tta atg cac agc ttt gag gat gct     723
Arg Pro Lys Asp Tyr Phe Asp Arg Leu Met His Ser Phe Glu Asp Ala
220             225             230             235

aaa ttg ttc cag acc tac cac gaa gat gac ctc cta gct act tgt atc     771
Lys Leu Phe Gln Thr Tyr His Glu Asp Asp Leu Leu Ala Thr Cys Ile
            240             245             250

ttg gtg agc tat aat aaa aaa tcc ttc tac atg tat gca gct tct tcc     819
Leu Val Ser Tyr Asn Lys Lys Ser Phe Tyr Met Tyr Ala Ala Ser Ser
            255             260             265

aac aaa aaa cga aat tta aat ggg tct ttg caa gaa aat tac gaa gcc     867
Asn Lys Lys Arg Asn Leu Asn Gly Ser Leu Gln Glu Asn Tyr Glu Ala
        270             275             280

atg aag tat gcc ttg gcc cga gga agc gaa gaa tat gat atg ggt ggg     915
Met Lys Tyr Ala Leu Ala Arg Gly Ser Glu Glu Tyr Asp Met Gly Gly
        285             290             295

gtc ttt ggc ttt gac aag tcg gac ggc ctc tac cgg ttt aaa aaa atc     963
Val Phe Gly Phe Asp Lys Ser Asp Gly Leu Tyr Arg Phe Lys Lys Ile
300             305             310             315

ttt acc ggt cat gaa ggg ctg aaa gaa ttt atg ggt gaa ttg gat gtg    1011
```

```
Phe Thr Gly His Glu Gly Leu Lys Glu Phe Met Gly Glu Leu Asp Val
          320               325               330

gtc tat gac caa gac cta tac gac gat ttt att tct taa                     1050
Val Tyr Asp Gln Asp Leu Tyr Asp Asp Phe Ile Ser
          335           340
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<210> 98
<211> 343
<212> PRT
<213> Alloiococcus otitidis

<400> 98
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Met Glu Glu Leu Ile Val Pro Leu Leu Asp Leu Asn Asp His Asp Arg
1             5               10               15


Val Gln Glu Tyr Glu Asp Phe Val Gln Asn His Pro Gln Gly His Leu
              20               25               30


Met Gln Ser Thr Lys Trp Ile Gln Val Lys Glu Gly Trp Asp Gly Asp
          35               40               45


Tyr Val Tyr Leu Thr Asp Asp Gln Asp Arg Ile Lys Ala Cys Leu Ser
      50               55               60


Ile Leu Ser Val Lys Asn Asp Gly Glu His Ala Phe Leu Tyr Ala Pro
65               70               75               80


Arg Gly Pro Val Cys Asp Phe His Asp Thr Asp Leu Val Thr Asp Leu
              85               90               95


Ile Lys Glu Ala Gln Val Val Ala Asp Lys His Lys Ala Phe Leu Leu
          100               105               110


Arg Met Asp Pro Glu Thr Leu His Asp Pro Asp Leu Val Glu Lys Tyr
      115               120               125


Arg Asp Leu Gly Tyr Thr Phe Arg Ser Ala Glu Gln Glu Asp Glu His
      130               135               140


Val Phe Ser Asn Pro Arg Phe His Met Met Thr Asp Leu Arg Gly His
145               150               155               160


Asp Glu Glu Ser Leu Leu Met Ala Phe Thr Ser Asn Asn Arg Arg Lys
              165               170               175
```

```
Ile Arg Lys Thr Tyr Lys Asn Asn Leu Gln Thr His Tyr Leu Thr Val
        180             185             190

Asp Asp Glu Gly Tyr Asp Gln Ala Leu Asp Asp Phe Tyr Glu Leu Thr
        195             200             205

Gln Ile Met Ala Glu Arg Gln Gly Ile Thr His Arg Pro Lys Asp Tyr
    210             215             220

Phe Asp Arg Leu Met His Ser Phe Glu Asp Ala Lys Leu Phe Gln Thr
225             230             235             240

Tyr His Glu Asp Asp Leu Leu Ala Thr Cys Ile Leu Val Ser Tyr Asn
            245             250             255

Lys Lys Ser Phe Tyr Met Tyr Ala Ala Ser Ser Asn Lys Lys Arg Asn
        260             265             270

Leu Asn Gly Ser Leu Gln Glu Asn Tyr Glu Ala Met Lys Tyr Ala Leu
    275             280             285

Ala Arg Gly Ser Glu Glu Tyr Asp Met Gly Gly Val Phe Gly Phe Asp
    290             295             300

Lys Ser Asp Gly Leu Tyr Arg Phe Lys Lys Ile Phe Thr Gly His Glu
305             310             315             320

Gly Leu Lys Glu Phe Met Gly Glu Leu Asp Val Val Tyr Asp Gln Asp
        325             330             335

Leu Tyr Asp Asp Phe Ile Ser
        340
```

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<210> 99
<211> 2244
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (22)..(2244)
<223>

<400> 99
ttacgtgaaa ggaagacttg c atg ggc cta gca aaa gat att tta ggc aaa       51
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                            Met Gly Leu Ala Lys Asp Ile Leu Gly Lys
                            1               5               10

atg aat gac aaa caa aaa caa gcg gtc atg acc act gat ggc cct ctc          99
Met Asn Asp Lys Gln Lys Gln Ala Val Met Thr Thr Asp Gly Pro Leu
            15              20              25

ttg atc atg gct ggg gca gga tct ggc aag acc cgg gtc tta acc cac         147
Leu Ile Met Ala Gly Ala Gly Ser Gly Lys Thr Arg Val Leu Thr His
            30              35              40

cgg ata gct tac ttg atc caa gaa aaa ggg gtt aat cct tgg aat atc         195
Arg Ile Ala Tyr Leu Ile Gln Glu Lys Gly Val Asn Pro Trp Asn Ile
            45              50              55

tta gcc atc acc ttt acc aac aag gcg gct ggc gag atg aaa gac cgg         243
Leu Ala Ile Thr Phe Thr Asn Lys Ala Ala Gly Glu Met Lys Asp Arg
        60              65              70

gtc cag aaa ctg gtt agc cag gga gga tct gga gtt tgg gtc tcg act         291
Val Gln Lys Leu Val Ser Gln Gly Gly Ser Gly Val Trp Val Ser Thr
75              80              85              90

ttc cac tct atg tgt gtt cgc att cta aga agg gac ggg gac caa att         339
Phe His Ser Met Cys Val Arg Ile Leu Arg Arg Asp Gly Asp Gln Ile
                95              100             105

ggc tat aac cgt gcc ttc acc att gct gac cct agt gaa cag aaa agt         387
Gly Tyr Asn Arg Ala Phe Thr Ile Ala Asp Pro Ser Glu Gln Lys Ser
            110             115             120

ttg atg aag cag gtc tta aaa gac ttg aat att gat cct aaa cgt tac         435
Leu Met Lys Gln Val Leu Lys Asp Leu Asn Ile Asp Pro Lys Arg Tyr
            125             130             135

aac ccc aag gcg ata ttg gcc gag att tcc aat gcc aaa aat gac ctc         483
Asn Pro Lys Ala Ile Leu Ala Glu Ile Ser Asn Ala Lys Asn Asp Leu
        140             145             150

ttg gat gag caa acc tac cgg aaa caa gct gat gac tat ttt aag gaa         531
Leu Asp Glu Gln Thr Tyr Arg Lys Gln Ala Asp Asp Tyr Phe Lys Glu
155             160             165             170

gtg gtg gct gac tgc tac gat gct tac caa aga cag ctc cgc cag tct         579
Val Val Ala Asp Cys Tyr Asp Ala Tyr Gln Arg Gln Leu Arg Gln Ser
            175             180             185

gag gcc atg gac ttt gac gac ctg att atg caa acc gtc cgt ctc ttc         627
Glu Ala Met Asp Phe Asp Asp Leu Ile Met Gln Thr Val Arg Leu Phe
            190             195             200

aag gaa aag ccc gat acc ctg tct tac tac cag gcc aag ttc cag tat         675
Lys Glu Lys Pro Asp Thr Leu Ser Tyr Tyr Gln Ala Lys Phe Gln Tyr
            205             210             215

atc cat gtt gac gaa tac cag gat acc aac caa gcc caa tac caa ctg         723
Ile His Val Asp Glu Tyr Gln Asp Thr Asn Gln Ala Gln Tyr Gln Leu
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                 220                      225                      230

gtt caa ctg cta gcc caa cgc ttt aaa aat gtt tgc gtc gtg gga gat      771
Val Gln Leu Leu Ala Gln Arg Phe Lys Asn Val Cys Val Val Gly Asp
235                 240                 245                 250

gct gac cag tct att tat ggt tgg cgg ggg gct gat atg gga aat att      819
Ala Asp Gln Ser Ile Tyr Gly Trp Arg Gly Ala Asp Met Gly Asn Ile
                255                 260                 265

ttg aat ttc gaa aaa gac tat cca gaa gcc caa acc atc ttt ttg gaa      867
Leu Asn Phe Glu Lys Asp Tyr Pro Glu Ala Gln Thr Ile Phe Leu Glu
                270                 275                 280

caa aat tac cgg tca acc aag tct ata atc agg gca gcc aat gat gtt      915
Gln Asn Tyr Arg Ser Thr Lys Ser Ile Ile Arg Ala Ala Asn Asp Val
                285                 290                 295

atc caa aac aat atc aac cgc cgg gac aag aat ttg tgg act gcc aac      963
Ile Gln Asn Asn Ile Asn Arg Arg Asp Lys Asn Leu Trp Thr Ala Asn
                300                 305                 310 .

gat gag ggg gac aag gtc agc tta tac gct gcc cgg agc gag cag gat     1011
Asp Glu Gly Asp Lys Val Ser Leu Tyr Ala Ala Arg Ser Glu Gln Asp
315                 320                 325                 330

gaa gcc cag ttt atc gta ggg acc atc cat gac cta aca gaa ggc aaa     1059
Glu Ala Gln Phe Ile Val Gly Thr Ile His Asp Leu Thr Glu Gly Lys
                335                 340 .               345

aag gct ggc tat ggg gac atc gcc atc ctc tac cgg acc aat gcc atg     1107
Lys Ala Gly Tyr Gly Asp Ile Ala Ile Leu Tyr Arg Thr Asn Ala Met
                350                 355                 360

tcc cgg gtt att gaa gaa acc ttt atc aag tcg aat atc ccc tac aag     1155
Ser Arg Val Ile Glu Glu Thr Phe Ile Lys Ser Asn Ile Pro Tyr Lys
                365                 370                 375

atc gtc ggc gga acc ggc ttt tac caa aga aaa gaa atc cgt gac ctg .   1203
Ile Val Gly Gly Thr Gly Phe Tyr Gln Arg Lys Glu Ile Arg Asp Leu
                380                 385                 390

att gcc tac cta acc cta gtg gct aac cca gct gat gac ctg tcc ttt     1251
Ile Ala Tyr Leu Thr Leu Val Ala Asn Pro Ala Asp Asp Leu Ser Phe
395                 400                 405                 410

tca cgg atc gtt aat gag ccc aaa aga ggg att gga ccc ggc acc ctg     1299
Ser Arg Ile Val Asn Glu Pro Lys Arg Gly Ile Gly Pro Gly Thr Leu
                415                 420                 425

gac aag tta cgc cag gct ggc cag gag atg ggt tgg tcg ctt tac gaa     1347
Asp Lys Leu Arg Gln Ala Gly Gln Glu Met Gly Trp Ser Leu Tyr Glu
                430                 435                 440

aca gct ctc aat gcg gat gct acc aac ctg cct agt cgg gct gtc aac     1395
Thr Ala Leu Asn Ala Asp Ala Thr Asn Leu Pro Ser Arg Ala Val Asn
                445                 450                 455
```

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aga cta tta gac ttc agt caa atg att gaa aat ttc agg aaa atg acg    1443
Arg Leu Leu Asp Phe Ser Gln Met Ile Glu Asn Phe Arg Lys Met Thr
    460             465             470

gaa tac tta ccg att act gat ttg acc gaa aaa atc tta gag gat act    1491
Glu Tyr Leu Pro Ile Thr Asp Leu Thr Glu Lys Ile Leu Glu Asp Thr
475             480             485             490

ggc tac caa aaa gcc tta gaa aaa gac cgg act ctt gaa tct cag gca    1539
Gly Tyr Gln Lys Ala Leu Glu Lys Asp Arg Thr Leu Glu Ser Gln Ala
            495             500             505

agg tta gag aac cta cag gaa ttt tac tcc gtc acc cag gaa ttt gac    1587
Arg Leu Glu Asn Leu Gln Glu Phe Tyr Ser Val Thr Gln Glu Phe Asp
            510             515             520

cag caa gaa gac gac aac aag tca ctc tta gcc ttc tta act gac ctt    1635
Gln Gln Glu Asp Asp Asn Lys Ser Leu Leu Ala Phe Leu Thr Asp Leu
        525             530             535

tcc tta ttg tca cca gct gat gat gtt gaa gag ggt cgg ggc cag gtc    1683
Ser Leu Leu Ser Pro Ala Asp Asp Val Glu Glu Gly Arg Gly Gln Val
        540             545             550

acc atg atg acc ctc cat gca gcc aag ggg ttg gaa ttc ccc tat gtc    1731
Thr Met Met Thr Leu His Ala Ala Lys Gly Leu Glu Phe Pro Tyr Val
555             560             565             570

ttt atc gct ggt atg gaa gag gga atc ttc ccc ttg tcc cgg gcg gct    1779
Phe Ile Ala Gly Met Glu Glu Gly Ile Phe Pro Leu Ser Arg Ala Ala
            575             580             585

gaa gac ccg gaa agc ttg gaa gaa gag cga cga ctg gcc tat gta ggg    1827
Glu Asp Pro Glu Ser Leu Glu Glu Glu Arg Arg Leu Ala Tyr Val Gly
            590             595             600

att acc cgg gct gag cag gcc ctc tac cta acc cgt gcc atg atg cgc    1875
Ile Thr Arg Ala Glu Gln Ala Leu Tyr Leu Thr Arg Ala Met Met Arg
        605             610             615

caa ctc tat ggc cgg acc cag gct aat ccc aaa tct cgc ttt tta tct    1923
Gln Leu Tyr Gly Arg Thr Gln Ala Asn Pro Lys Ser Arg Phe Leu Ser
    620             625             630

gaa att tct tct gac ctg gtc caa gac ctt ggt gct aca act ggg tct    1971
Glu Ile Ser Ser Asp Leu Val Gln Asp Leu Gly Ala Thr Thr Gly Ser
635             640             645             650

ctt agc cag act ggg ggg aaa gtt agc cct aga cta gga ggc cgc aaa    2019
Leu Ser Gln Thr Gly Gly Lys Val Ser Pro Arg Leu Gly Gly Arg Lys
            655             660             665

gcc agt ggt tat aag gct aat gct tgg tct cag caa tca gtt ggg gcg    2067
Ala Ser Gly Tyr Lys Ala Asn Ala Trp Ser Gln Gln Ser Val Gly Ala
            670             675             680
```

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act ggg gct gaa aaa gaa gac tgg gaa gtt ggt gac aag gtc cac cac      2115
Thr Gly Ala Glu Lys Glu Asp Trp Glu Val Gly Asp Lys Val His His
        685                 690                 695

aaa aaa tgg ggc caa gga acc att att gag att aaa ggt tct ggc tcg      2163
Lys Lys Trp Gly Gln Gly Thr Ile Ile Glu Ile Lys Gly Ser Gly Ser
        700                 705                 710

gac ctc cag ctc aac att gcc ttt cca gat gaa ggg atc aag ccc ttg      2211
Asp Leu Gln Leu Asn Ile Ala Phe Pro Asp Glu Gly Ile Lys Pro Leu
715                 720                 725                 730

cta gcc agt ttt gcc ccc atc gaa aag att tag                          2244
Leu Ala Ser Phe Ala Pro Ile Glu Lys Ile
                735                 740
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<210> 100
<211> 740
<212> PRT
<213> Alloiococcus otitidis

<400> 100
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Met Gly Leu Ala Lys Asp Ile Leu Gly Lys Met Asn Asp Lys Gln Lys
1               5                   10                  15


Gln Ala Val Met Thr Thr Asp Gly Pro Leu Leu Ile Met Ala Gly Ala
            20                  25                  30


Gly Ser Gly Lys Thr Arg Val Leu Thr His Arg Ile Ala Tyr Leu Ile
        35                  40                  45


Gln Glu Lys Gly Val Asn Pro Trp Asn Ile Leu Ala Ile Thr Phe Thr
    50                  55                  60


Asn Lys Ala Ala Gly Glu Met Lys Asp Arg Val Gln Lys Leu Val Ser
65                  70                  75                  80


Gln Gly Gly Ser Gly Val Trp Val Ser Thr Phe His Ser Met Cys Val
                85                  90                  95


Arg Ile Leu Arg Arg Asp Gly Asp Gln Ile Gly Tyr Asn Arg Ala Phe
            100                 105                 110


Thr Ile Ala Asp Pro Ser Glu Gln Lys Ser Leu Met Lys Gln Val Leu
        115                 120                 125


Lys Asp Leu Asn Ile Asp Pro Lys Arg Tyr Asn Pro Lys Ala Ile Leu
    130                 135                 140
```

```
Ala Glu Ile Ser Asn Ala Lys Asn Asp Leu Leu Asp Glu Gln Thr Tyr
145             150             155             160

Arg Lys Gln Ala Asp Asp Tyr Phe Lys Glu Val Val Ala Asp Cys Tyr
        165             170             175

Asp Ala Tyr Gln Arg Gln Leu Arg Gln Ser Glu Ala Met Asp Phe Asp
        180             185             190

Asp Leu Ile Met Gln Thr Val Arg Leu Phe Lys Glu Lys Pro Asp Thr
        195             200             205

Leu Ser Tyr Tyr Gln Ala Lys Phe Gln Tyr Ile His Val Asp Glu Tyr
    210             215             220

Gln Asp Thr Asn Gln Ala Gln Tyr Gln Leu Val Gln Leu Leu Ala Gln
225             230             235             240

Arg Phe Lys Asn Val Cys Val Val Gly Asp Ala Asp Gln Ser Ile Tyr
        245             250             255

Gly Trp Arg Gly Ala Asp Met Gly Asn Ile Leu Asn Phe Glu Lys Asp
        260             265             270

Tyr Pro Glu Ala Gln Thr Ile Phe Leu Glu Gln Asn Tyr Arg Ser Thr
    275             280             285

Lys Ser Ile Ile Arg Ala Ala Asn Asp Val Ile Gln Asn Asn Ile Asn
    290             295             300

Arg Arg Asp Lys Asn Leu Trp Thr Ala Asn Asp Glu Gly Asp Lys Val
305             310             315             320

Ser Leu Tyr Ala Ala Arg Ser Glu Gln Asp Glu Ala Gln Phe Ile Val
        325             330             335

Gly Thr Ile His Asp Leu Thr Glu Gly Lys Lys Ala Gly Tyr Gly Asp
        340             345             350

Ile Ala Ile Leu Tyr Arg Thr Asn Ala Met Ser Arg Val Ile Glu Glu
    355             360             365
```

Thr Phe Ile Lys Ser Asn Ile Pro Tyr Lys Ile Val Gly Gly Thr Gly
370   375   380

Phe Tyr Gln Arg Lys Glu Ile Arg Asp Leu Ile Ala Tyr Leu Thr Leu
385   390   395   400

Val Ala Asn Pro Ala Asp Asp Leu Ser Phe Ser Arg Ile Val Asn Glu
          405   410   415

Pro Lys Arg Gly Ile Gly Pro Gly Thr Leu Asp Lys Leu Arg Gln Ala
          420   425   430

Gly Gln Glu Met Gly Trp Ser Leu Tyr Glu Thr Ala Leu Asn Ala Asp
          435   440   445

Ala Thr Asn Leu Pro Ser Arg Ala Val Asn Arg Leu Leu Asp Phe Ser
     450   455   460

Gln Met Ile Glu Asn Phe Arg Lys Met Thr Glu Tyr Leu Pro Ile Thr
465   470   475   480

Asp Leu Thr Glu Lys Ile Leu Glu Asp Thr Gly Tyr Gln Lys Ala Leu
          485   490   495

Glu Lys Asp Arg Thr Leu Glu Ser Gln Ala Arg Leu Glu Asn Leu Gln
          500   505   510

Glu Phe Tyr Ser Val Thr Gln Glu Phe Asp Gln Gln Glu Asp Asp Asn
          515   520   525

Lys Ser Leu Leu Ala Phe Leu Thr Asp Leu Ser Leu Leu Ser Pro Ala
     530   535   540

Asp Asp Val Glu Glu Gly Arg Gly Gln Val Thr Met Met Thr Leu His
545   550   555   560

Ala Ala Lys Gly Leu Glu Phe Pro Tyr Val Phe Ile Ala Gly Met Glu
          565   570   575

Glu Gly Ile Phe Pro Leu Ser Arg Ala Ala Glu Asp Pro Glu Ser Leu
          580   585   590

```
Glu Glu Glu Arg Arg Leu Ala Tyr Val Gly Ile Thr Arg Ala Glu Gln
        595             600             605

Ala Leu Tyr Leu Thr Arg Ala Met Met Arg Gln Leu Tyr Gly Arg Thr
    610             615             620

Gln Ala Asn Pro Lys Ser Arg Phe Leu Ser Glu Ile Ser Ser Asp Leu
625             630             635             640

Val Gln Asp Leu Gly Ala Thr Thr Gly Ser Leu Ser Gln Thr Gly Gly
            645             650             655

Lys Val Ser Pro Arg Leu Gly Gly Arg Lys Ala Ser Gly Tyr Lys Ala
            660             665             670

Asn Ala Trp Ser Gln Gln Ser Val Gly Ala Thr Gly Ala Glu Lys Glu
        675             680             685

Asp Trp Glu Val Gly Asp Lys Val His His Lys Lys Trp Gly Gln Gly
    690             695             700

Thr Ile Ile Glu Ile Lys Gly Ser Gly Ser Asp Leu Gln Leu Asn Ile
705             710             715             720

Ala Phe Pro Asp Glu Gly Ile Lys Pro Leu Leu Ala Ser Phe Ala Pro
            725             730             735

Ile Glu Lys Ile
            740


<210> 101
<211> 1314
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (4)..(1314)
<223>

<400> 101
agt atg gac aca atc gtc att caa gga gga gac aat cga ctt gag ggt      48
    Met Asp Thr Ile Val Ile Gln Gly Gly Asp Asn Arg Leu Glu Gly
    1               5                   10                  15

aca gtc aag gta gaa ggg gct aag aat gct gcc ctt cct atc ctg gct      96
Thr Val Lys Val Glu Gly Ala Lys Asn Ala Ala Leu Pro Ile Leu Ala
```

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                        20                    25                    30

gcc agt ctt tta cca gaa gat ggg aaa agt cac ctg tcc aat gtc ccc          144
Ala Ser Leu Leu Pro Glu Asp Gly Lys Ser His Leu Ser Asn Val Pro
        35                    40                    45

tta cta tct gat att tac acg atg caa gaa gtt ttg cgt tac tta aac          192
Leu Leu Ser Asp Ile Tyr Thr Met Gln Glu Val Leu Arg Tyr Leu Asn          .
        50                    55                    60

gtt gac att gac ttc gat gaa gac cac aac gaa atc gtc ata gat gct          240
Val Asp Ile Asp Phe Asp Glu Asp His Asn Glu Ile Val Ile Asp Ala
    65                    70                    75

aca gga gac ctg aat tcc aat acc cct tat gaa ttt atg agc aag atg          288
Thr Gly Asp Leu Asn Ser Asn Thr Pro Tyr Glu Phe Met Ser Lys Met
80                    85                    90                    95

cgg gct tcc atc att gtc atg ggt ccc tta cta gcc cgt aat ggt tat          336
Arg Ala Ser Ile Ile Val Met Gly Pro Leu Leu Ala Arg Asn Gly Tyr
                100                    105                    110

gcc aaa gtc gct ctt cct ggt ggt tgc gcg att ggg act cgt cct att          384
Ala Lys Val Ala Leu Pro Gly Gly Cys Ala Ile Gly Thr Arg Pro Ile
                115                    120                    125

gac ttg cac tta aaa ggc ttc cgg gct atg ggg gtc gat gtg gaa gtc          432
Asp Leu His Leu Lys Gly Phe Arg Ala Met Gly Val Asp Val Glu Val
        130                    135                    140

gaa gga ggt tat gtg atc gcc aca gtt caa gat gaa ctg gat ggc gct          480
Glu Gly Gly Tyr Val Ile Ala Thr Val Gln Asp Glu Leu Asp Gly Ala
    145                    150                    155

gat att tac ctt gac ttc cca agt gtt gga gct aca caa aat att ttg          528
Asp Ile Tyr Leu Asp Phe Pro Ser Val Gly Ala Thr Gln Asn Ile Leu
160                    165                    170                    175

atg gct gcc acc cgg gca aaa ggg aca aca gtc atc gag aat gca gct          576
Met Ala Ala Thr Arg Ala Lys Gly Thr Thr Val Ile Glu Asn Ala Ala
                180                    185                    190

cga gaa cct gaa att gtt gac ctt gcc aac tat ttg aac aag atg ggt          624
Arg Glu Pro Glu Ile Val Asp Leu Ala Asn Tyr Leu Asn Lys Met Gly
                195                    200                    205

gcc cgt att tac ggg gcc gga acc aat acc atg aga att gaa ggg gta          672
Ala Arg Ile Tyr Gly Ala Gly Thr Asn Thr Met Arg Ile Glu Gly Val
                210                    215                    220

gac aag cta gaa gct tgt gac cac tcc att att gcc gac cgg ata gaa          720
Asp Lys Leu Glu Ala Cys Asp His Ser Ile Ile Ala Asp Arg Ile Glu
        225                    230                    235

agt ggc acc ttt atg gta gca gct ggt gtc acc caa ggg aat gtc ttg          768
Ser Gly Thr Phe Met Val Ala Ala Gly Val Thr Gln Gly Asn Val Leu
240                    245                    250                    255
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att gaa gac tgt atc gtc gaa cac aac cgc ccc tta att tcc aag tta      816
Ile Glu Asp Cys Ile Val Glu His Asn Arg Pro Leu Ile Ser Lys Leu
                260                 265                 270

agt gaa atg ggc gtt caa ttt gag gaa gaa aaa acc ggc ctt cga gtc      864
Ser Glu Met Gly Val Gln Phe Glu Glu Glu Lys Thr Gly Leu Arg Val
                275                 280                 285

atg gga cca gag acc tta cag gca aca gat gtt aaa acc ctg cct tat      912
Met Gly Pro Glu Thr Leu Gln Ala Thr Asp Val Lys Thr Leu Pro Tyr
                290                 295                 300

cct ggc ttc cca act gat atg cag tca ccg atg aca gtc gcc caa acc      960
Pro Gly Phe Pro Thr Asp Met Gln Ser Pro Met Thr Val Ala Gln Thr
                305                 310                 315

cta gct gag gga aga agc atc atg aga gaa acg gtc ttc gaa aac cgc     1008
Leu Ala Glu Gly Arg Ser Ile Met Arg Glu Thr Val Phe Glu Asn Arg
320                 325                 330                 335

ttc atg cac atg gaa gag ctt cgt aaa atg gat gca caa ttt act gtc     1056
Phe Met His Met Glu Glu Leu Arg Lys Met Asp Ala Gln Phe Thr Val
                340                 345                 350

gat ggc cag tcc ctt att atc gag ggg ggc aaa aaa ctc caa ggt gct     1104
Asp Gly Gln Ser Leu Ile Ile Glu Gly Gly Lys Lys Leu Gln Gly Ala
                355                 360                 365

aga gtc cag tcc agt gac ttg cgg gct tca gct tcc ttg att att gct     1152
Arg Val Gln Ser Ser Asp Leu Arg Ala Ser Ala Ser Leu Ile Ile Ala
                370                 375                 380

ggt tta gta gct gat ggt gtc acc aaa gta acc aat ctt aac cac tta     1200
Gly Leu Val Ala Asp Gly Val Thr Lys Val Thr Asn Leu Asn His Leu
                385                 390                 395

gac cgg ggc tac tat aaa ttt cac gaa aaa tta cag caa tta ggt gct     1248
Asp Arg Gly Tyr Tyr Lys Phe His Glu Lys Leu Gln Gln Leu Gly Ala
400                 405                 410                 415

tcc att gaa cga atc gac gag gaa att caa gtt gac cag gaa gcc agc     1296
Ser Ile Glu Arg Ile Asp Glu Glu Ile Gln Val Asp Gln Glu Ala Ser
                420                 425                 430

ctc aaa aaa ggc gaa taa                                             1314
Leu Lys Lys Gly Glu
                435
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<210> 102
<211> 436
<212> PRT
<213> Alloiococcus otitidis

<400> 102
Met Asp Thr Ile Val Ile Gln Gly Gly Asp Asn Arg Leu Glu Gly Thr
```

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1                 5                      10                     15


Val Lys Val Glu Gly Ala Lys Asn Ala Ala Leu Pro Ile Leu Ala Ala
            20              25                  30


Ser Leu Leu Pro Glu Asp Gly Lys Ser His Leu Ser Asn Val Pro Leu
            35              40                  45


Leu Ser Asp Ile Tyr Thr Met Gln Glu Val Leu Arg Tyr Leu Asn Val
            50              55                  60


Asp Ile Asp Phe Asp Glu Asp His Asn Glu Ile Val Ile Asp Ala Thr
65              70                  75                  80


Gly Asp Leu Asn Ser Asn Thr Pro Tyr Glu Phe Met Ser Lys Met Arg
                85                  90                  95


Ala Ser Ile Ile Val Met Gly Pro Leu Leu Ala Arg Asn Gly Tyr Ala
                100                 105                 110


Lys Val Ala Leu Pro Gly Gly Cys Ala Ile Gly Thr Arg Pro Ile Asp
            115             120                 125


Leu His Leu Lys Gly Phe Arg Ala Met Gly Val Asp Val Glu Val Glu
    130                 135                 140


Gly Gly Tyr Val Ile Ala Thr Val Gln Asp Glu Leu Asp Gly Ala Asp
145                 150                 155                 160


Ile Tyr Leu Asp Phe Pro Ser Val Gly Ala Thr Gln Asn Ile Leu Met
                165                 170                 175


Ala Ala Thr Arg Ala Lys Gly Thr Thr Val Ile Glu Asn Ala Ala Arg
            180             185                 190


Glu Pro Glu Ile Val Asp Leu Ala Asn Tyr Leu Asn Lys Met Gly Ala
        195                 200                 205


Arg Ile Tyr Gly Ala Gly Thr Asn Thr Met Arg Ile Glu Gly Val Asp
    210                 215                 220


Lys Leu Glu Ala Cys Asp His Ser Ile Ile Ala Asp Arg Ile Glu Ser
225                 230                 235                 240
```

Gly Thr Phe Met Val Ala Ala Gly Val Thr Gln Gly Asn Val Leu Ile
            245   250   255

Glu Asp Cys Ile Val Glu His Asn Arg Pro Leu Ile Ser Lys Leu Ser
            260   265   270

Glu Met Gly Val Gln Phe Glu Glu Glu Lys Thr Gly Leu Arg Val Met
            275   280   285

Gly Pro Glu Thr Leu Gln Ala Thr Asp Val Lys Thr Leu Pro Tyr Pro
    290   295   300

Gly Phe Pro Thr Asp Met Gln Ser Pro Met Thr Val Ala Gln Thr Leu
305   310   315   320

Ala Glu Gly Arg Ser Ile Met Arg Glu Thr Val Phe Glu Asn Arg Phe
            325   330   335

Met His Met Glu Glu Leu Arg Lys Met Asp Ala Gln Phe Thr Val Asp
            340   345   350

Gly Gln Ser Leu Ile Ile Glu Gly Gly Lys Lys Leu Gln Gly Ala Arg
            355   360   365

Val Gln Ser Ser Asp Leu Arg Ala Ser Ala Ser Leu Ile Ile Ala Gly
    370   375   380

Leu Val Ala Asp Gly Val Thr Lys Val Thr Asn Leu Asn His Leu Asp
385   390   395   400

Arg Gly Tyr Tyr Lys Phe His Glu Lys Leu Gln Gln Leu Gly Ala Ser
            405   410   415

Ile Glu Arg Ile Asp Glu Glu Ile Gln Val Asp Gln Glu Ala Ser Leu
            420   425   430

Lys Lys Gly Glu
        435

<210> 103
<211> 1026
<212> DNA

<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (34)..(1026)
<223>

<400> 103
acagttttaa tccagttagc cacaaggtgg gat atg atg gac tta gca gaa aaa   54
                                    Met Met Asp Leu Ala Glu Lys
                                    1   5

caa gca ggg gtc tac caa ctt ttt gac cga atc ctg gcc aac cat gcc   102
Gln Ala Gly Val Tyr Gln Leu Phe Asp Arg Ile Leu Ala Asn His Ala
        10   15   20

ctc aag cat gcc tat ctt ttt gaa ggt ttg gcc gga tca ggc aaa ctg   150
Leu Lys His Ala Tyr Leu Phe Glu Gly Leu Ala Gly Ser Gly Lys Leu
    25   30   35

gag atg agc cgg tat att gcc aag aga ctg ttt tgc ccc aac caa gac   198
Glu Met Ser Arg Tyr Ile Ala Lys Arg Leu Phe Cys Pro Asn Gln Asp
40   45   50   55

cag gga caa gct tgc caa gtt tgt ccc act tgc ttg cgc att gac cag   246
Gln Gly Gln Ala Cys Gln Val Cys Pro Thr Cys Leu Arg Ile Asp Gln
                60   65   70

ggt caa cac cct gat gtg gta gaa ata gcc cct gag ggg aag gga cgg   294
Gly Gln His Pro Asp Val Val Glu Ile Ala Pro Glu Gly Lys Gly Arg
                75   80   85

tcg att agg gta gac cgg gta cga cag gtc aag gat gcc cta agc aag   342
Ser Ile Arg Val Asp Arg Val Arg Gln Val Lys Asp Ala Leu Ser Lys
        90   95   100

tct ggt gtg gag agt caa aag aaa atg att atc ctt aac cag gct gat   390
Ser Gly Val Glu Ser Gln Lys Lys Met Ile Ile Leu Asn Gln Ala Asp
        105   110   115

aaa atg acc ccc agt gca gcc aac agc ctg ctt aaa ttt ctg gaa gag   438
Lys Met Thr Pro Ser Ala Ala Asn Ser Leu Leu Lys Phe Leu Glu Glu
120   125   130   135

ccg gca ggg gat gtg act att ttc ttg tta gtt act agc cgg caa aac   486
Pro Ala Gly Asp Val Thr Ile Phe Leu Leu Val Thr Ser Arg Gln Asn
                140   145   150

ctt ttg cca act att gtt tcc cgc tgc cag gtt atc cag ttt gcc aag   534
Leu Leu Pro Thr Ile Val Ser Arg Cys Gln Val Ile Gln Phe Ala Lys
                155   160   165

cag gat tta aag act cgg att gag gac tta gtg gaa gcc ggt ttg tcc   582
Gln Asp Leu Lys Thr Arg Ile Glu Asp Leu Val Glu Ala Gly Leu Ser
                170   175   180

cag gaa gaa gcc cac ttg gcc agc cac ctc agc caa gac tta gac ttg   630

```
      Gln Glu Glu Ala His Leu Ala Ser His Leu Ser Gln Asp Leu Asp Leu
          185                 190                 195

      gct aag tcc ctc att gag gaa gag gac ttg ctg gca gtc agt caa aaa    678
      Ala Lys Ser Leu Ile Glu Glu Glu Asp Leu Leu Ala Val Ser Gln Lys
      200                 205                 210                 215

      att tgg cag tgg ttt agc tat ctc atg aac caa gat gac ttg gcc ttt    726
      Ile Trp Gln Trp Phe Ser Tyr Leu Met Asn Gln Asp Asp Leu Ala Phe
                      220                 225                 230

      atc cta gtc caa aga gac tta atg gcc ttt atc caa gac cgg gat gac    774
      Ile Leu Val Gln Arg Asp Leu Met Ala Phe Ile Gln Asp Arg Asp Asp
                  235                 240                 245

      tgc cag atg gtt tgt gac tta atc ctc tac ctc ttc caa gac ctg ctc    822
      Cys Gln Met Val Cys Asp Leu Ile Leu Tyr Leu Phe Gln Asp Leu Leu
              250                 255                 260

      cac tta cac tac cat tta gat agt ccg gcc tgc ttc gca ggc cac gaa    870
      His Leu His Tyr His Leu Asp Ser Pro Ala Cys Phe Ala Gly His Glu
          265                 270                 275

      agt gac ctc cgc tac ttt atg gac ctg ctt tcg atc aag caa gtg tct    918
      Ser Asp Leu Arg Tyr Phe Met Asp Leu Leu Ser Ile Lys Gln Val Ser
      280                 285                 290                 295

      tat gcc atg caa gcc acc ctg caa gct aaa aga gaa gtg gac cac aat    966
      Tyr Ala Met Gln Ala Thr Leu Gln Ala Lys Arg Glu Val Asp His Asn
                      300                 305                 310

      gtg gcc agt cag gct gtt tta gaa ggc ttg act ttg gac ttg cag gaa    1014
      Val Ala Ser Gln Ala Val Leu Glu Gly Leu Thr Leu Asp Leu Gln Glu
                  315                 320                 325

      agt ata ggc taa                                                    1026
      Ser Ile Gly
              330


      <210> 104
      <211> 330
      <212> PRT
      <213> Alloiococcus otitidis

      <400> 104
      Met Met Asp Leu Ala Glu Lys Gln Ala Gly Val Tyr Gln Leu Phe Asp
      1               5                   10                  15


      Arg Ile Leu Ala Asn His Ala Leu Lys His Ala Tyr Leu Phe Glu Gly
                  20                  25                  30


      Leu Ala Gly Ser Gly Lys Leu Glu Met Ser Arg Tyr Ile Ala Lys Arg
              35                  40                  45
```

```
Leu Phe Cys Pro Asn Gln Asp Gln Gly Gln Ala Cys Gln Val Cys Pro
    50              55              60

Thr Cys Leu Arg Ile Asp Gln Gly Gln His Pro Asp Val Val Glu Ile
65              70              75              80

Ala Pro Glu Gly Lys Gly Arg Ser Ile Arg Val Asp Arg Val Arg Gln
            85              90              95

Val Lys Asp Ala Leu Ser Lys Ser Gly Val Glu Ser Gln Lys Lys Met
            100             105             110

Ile Ile Leu Asn Gln Ala Asp Lys Met Thr Pro Ser Ala Ala Asn Ser
        115             120             125

Leu Leu Lys Phe Leu Glu Glu Pro Ala Gly Asp Val Thr Ile Phe Leu
    130             135             140

Leu Val Thr Ser Arg Gln Asn Leu Leu Pro Thr Ile Val Ser Arg Cys
145             150             155             160

Gln Val Ile Gln Phe Ala Lys Gln Asp Leu Lys Thr Arg Ile Glu Asp
            165             170             175

Leu Val Glu Ala Gly Leu Ser Gln Glu Glu Ala His Leu Ala Ser His
            180             185             190

Leu Ser Gln Asp Leu Asp Leu Ala Lys Ser Leu Ile Glu Glu Glu Asp
        195             200             205

Leu Leu Ala Val Ser Gln Lys Ile Trp Gln Trp Phe Ser Tyr Leu Met
    210             215             220

Asn Gln Asp Asp Leu Ala Phe Ile Leu Val Gln Arg Asp Leu Met Ala
225             230             235             240

Phe Ile Gln Asp Arg Asp Asp Cys Gln Met Val Cys Asp Leu Ile Leu
            245             250             255

Tyr Leu Phe Gln Asp Leu Leu His Leu His Tyr His Leu Asp Ser Pro
            260             265             270
```

```
Ala Cys Phe Ala Gly His Glu Ser Asp Leu Arg Tyr Phe Met Asp Leu
        275                 280                 285


Leu Ser Ile Lys Gln Val Ser Tyr Ala Met Gln Ala Thr Leu Gln Ala
        290                 295                 300


Lys Arg Glu Val Asp His Asn Val Ala Ser Gln Ala Val Leu Glu Gly
305                 310                 315                 320


Leu Thr Leu Asp Leu Gln Glu Ser Ile Gly
                325                 330
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<210> 105
<211> 1785
<212> DNA
<213> Alloiococcus otitidis

<220>
<221> CDS
<222> (13)..(1785)
<223>

<400> 105
gaggggagag ct atg acc cac cag gcc tta tac cgg gta tgg cga ccg caa      51
            Met Thr His Gln Ala Leu Tyr Arg Val Trp Arg Pro Gln
             1               5                   10

agt ttt gct gat gta tcc ggc cag cat gtg gtc acc aag acc cta aag      99
Ser Phe Ala Asp Val Ser Gly Gln His Val Val Thr Lys Thr Leu Lys
    15                  20                  25

aat gcc att aaa aat gat aat acc agt cat gcc tac ctg ttt act gga     147
Asn Ala Ile Lys Asn Asp Asn Thr Ser His Ala Tyr Leu Phe Thr Gly
30                  35                  40                  45

ccc cgg ggg acg ggc aag acc agt gtg gca aaa ata ttt gcc aag gcc     195
Pro Arg Gly Thr Gly Lys Thr Ser Val Ala Lys Ile Phe Ala Lys Ala
                50                  55                  60

att aat tgc ccc tac tcg gat gat ggg gag cct tgt aat gaa tgt cag     243
Ile Asn Cys Pro Tyr Ser Asp Asp Gly Glu Pro Cys Asn Glu Cys Gln
                65                  70                  75

att tgc cag gag atc acc cag ggt agt cta ggc gat gtc atc gaa atc     291
Ile Cys Gln Glu Ile Thr Gln Gly Ser Leu Gly Asp Val Ile Glu Ile
            80                  85                  90

gat gcg gcc agc aat aat ggg gtg gaa gag att cgc gat att agg gaa     339
Asp Ala Ala Ser Asn Asn Gly Val Glu Glu Ile Arg Asp Ile Arg Glu
    95                  100                 105

aag gct aat tat gcc cca act tcg gcc gtt tac aag gtc tac att atc     387
Lys Ala Asn Tyr Ala Pro Thr Ser Ala Val Tyr Lys Val Tyr Ile Ile
```

```
            110                 115                 120                 125

gat gag gtc cat atg tta tcc tct ggg gcc ttt aac gcc ctc ttg aaa        435
Asp Glu Val His Met Leu Ser Ser Gly Ala Phe Asn Ala Leu Leu Lys
                130                 135                 140

aca ctg gaa gag cct cca gcc aat gtg gtc ttt atc tta gca acg act        483
Thr Leu Glu Glu Pro Pro Ala Asn Val Val Phe Ile Leu Ala Thr Thr
                145                 150                 155

gaa ccc cac aag att ccg gct acc att atc tcc cgg acc cag cgt ttt        531
Glu Pro His Lys Ile Pro Ala Thr Ile Ile Ser Arg Thr Gln Arg Phe
                160                 165                 170

gat ttt aag cgg att gac aac cag gac atc atc gac cgc ttg att tat        579
Asp Phe Lys Arg Ile Asp Asn Gln Asp Ile Ile Asp Arg Leu Ile Tyr
                175                 180                 185

atc tta gaa gaa gac cag gtc ccc tac agc aaa gaa gcc gtc cta agc        627
Ile Leu Glu Glu Asp Gln Val Pro Tyr Ser Lys Glu Ala Val Leu Ser
  190                 195                 200                 205

cta gcc aat gca gcg gaa ggt ggg atg cgg gat gcc ttg agt atg ttg        675
Leu Ala Asn Ala Ala Glu Gly Gly Met Arg Asp Ala Leu Ser Met Leu
                210                 215                 220

gac cag gcc tta agc ttt atg aca gat gag tta aca gaa gaa gtt gcc        723
Asp Gln Ala Leu Ser Phe Met Thr Asp Glu Leu Thr Glu Glu Val Ala
                225                 230                 235

ctc cag att aca ggg agc att acc cag tct ctc ttg ctt gaa tac ttg        771
Leu Gln Ile Thr Gly Ser Ile Thr Gln Ser Leu Leu Leu Glu Tyr Leu
                240                 245                 250

cag gtg att agc caa ggt cag acg gaa gaa gga ctc aag ctc ttg caa        819
Gln Val Ile Ser Gln Gly Gln Thr Glu Glu Gly Leu Lys Leu Leu Gln
                255                 260                 265

gaa gtt tta ggg gaa ggc aag gac cct agc cgg ttt gtg gaa gac gct        867
Glu Val Leu Gly Glu Gly Lys Asp Pro Ser Arg Phe Val Glu Asp Ala
  270                 275                 280                 285

att atg atg acc cgg gac ctc ttg ctt tac caa act agc caa ggc gat        915
Ile Met Met Thr Arg Asp Leu Leu Leu Tyr Gln Thr Ser Gln Gly Asp
                290                 295                 300

aat ttt gtt cct aaa ttg gct cgc tta gac gac cag ttt gaa gac ctg        963
Asn Phe Val Pro Lys Leu Ala Arg Leu Asp Asp Gln Phe Glu Asp Leu
                305                 310                 315

gcg aag gac ttg gac aag gag atg gcc tac cat att att gat gtc tta       1011
Ala Lys Asp Leu Asp Lys Glu Met Ala Tyr His Ile Ile Asp Val Leu
                320                 325                 330

aac caa acc caa gac gat ctc cgc cta agc aac cat ggg gaa gtc tat       1059
Asn Gln Thr Gln Asp Asp Leu Arg Leu Ser Asn His Gly Glu Val Tyr
                335                 340                 345
```

```
ttg gaa ata gcc acg gtc aag ctt agc cag cct tct tca gcc gtt cag        1107
Leu Glu Ile Ala Thr Val Lys Leu Ser Gln Pro Ser Ser Ala Val Gln
350             355             360             365

acc atc cag gcc agc caa gtc aac atg gtg gac cag gat aat aaa gaa        1155
Thr Ile Gln Ala Ser Gln Val Asn Met Val Asp Gln Asp Asn Lys Glu
                370             375             380

gag att gcc caa ctg caa aac cag gtc aag tcc ctc cag caa agt att        1203
Glu Ile Ala Gln Leu Gln Asn Gln Val Lys Ser Leu Gln Gln Ser Ile
            385             390             395

caa aac ttg caa gct gga gcc aaa caa ggg cct aag caa aga gct aag        1251
Gln Asn Leu Gln Ala Gly Ala Lys Gln Gly Pro Lys Gln Arg Ala Lys
        400             405             410

tca aaa gct ggc ccc aag caa tct ggc cct ggc aag tct aga agc cac        1299
Ser Lys Ala Gly Pro Lys Gln Ser Gly Pro Gly Lys Ser Arg Ser His
        415             420             425

cgt cac cag caa ggc ttc aag gtt aac cgg aaa gcc gtt tac tct atc        1347
Arg His Gln Gln Gly Phe Lys Val Asn Arg Lys Ala Val Tyr Ser Ile
430             435             440             445

ttg gac cag gcg acc cgt aaa gac ctg gac gac ctc caa gac ctc tgg        1395
Leu Asp Gln Ala Thr Arg Lys Asp Leu Asp Asp Leu Gln Asp Leu Trp
            450             455             460

cca gac ttg atc aat gtc ttg acc atc agt caa aag gct atc tta aac        1443
Pro Asp Leu Ile Asn Val Leu Thr Ile Ser Gln Lys Ala Ile Leu Asn
            465             470             475

aat tcc aaa cca gtt gct gct agt cca gag ggt ttg gtg gtg acc ttt        1491
Asn Ser Lys Pro Val Ala Ala Ser Pro Glu Gly Leu Val Val Thr Phe
        480             485             490

gaa tat gat att cta tgt gag aga gca gag tct gac gag acc ttg caa        1539
Glu Tyr Asp Ile Leu Cys Glu Arg Ala Glu Ser Asp Glu Thr Leu Gln
        495             500             505

acg gct atc ggc aat tac atc gaa aaa att atc ggc cgc cgt cca aga        1587
Thr Ala Ile Gly Asn Tyr Ile Glu Lys Ile Ile Gly Arg Arg Pro Arg
510             515             520             525

ctg gtc tgt gtg cct gaa gac aag tgg ccg act atc cgc cgc gat ttt        1635
Leu Val Cys Val Pro Glu Asp Lys Trp Pro Thr Ile Arg Arg Asp Phe
            530             535             540

atc aag cag atg aaa aaa gaa gat ggc agt act aaa gct ggc caa gca        1683
Ile Lys Gln Met Lys Lys Glu Asp Gly Ser Thr Lys Ala Gly Gln Ala
            545             550             555

agt gac ggc aag tcg gat gat gac cca ggt caa gaa gac aac cag gcc        1731
Ser Asp Gly Lys Ser Asp Asp Asp Pro Gly Gln Glu Asp Asn Gln Ala
            560             565             570
```

```
ctt aac aag gct gtg gag ctt ttc ggt aaa gac aat att aca atc aaa    1779
Leu Asn Lys Ala Val Glu Leu Phe Gly Lys Asp Asn Ile Thr Ile Lys
    575                 580                 585

gat taa                                                            1785
Asp
590
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<210> 106
<211> 590
<212> PRT
<213> Alloiococcus otitidis

<400> 106

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Met Thr His Gln Ala Leu Tyr Arg Val Trp Arg Pro Gln Ser Phe Ala
1               5                10                15


Asp Val Ser Gly Gln His Val Val Thr Lys Thr Leu Lys Asn Ala Ile
            20                25                30


Lys Asn Asp Asn Thr Ser His Ala Tyr Leu Phe Thr Gly Pro Arg Gly
        35                40                45


Thr Gly Lys Thr Ser Val Ala Lys Ile Phe Ala Lys Ala Ile Asn Cys
    50                55                60


Pro Tyr Ser Asp Asp Gly Glu Pro Cys Asn Glu Cys Gln Ile Cys Gln
65                70                75                80


Glu Ile Thr Gln Gly Ser Leu Gly Asp Val Ile Glu Ile Asp Ala Ala
                85                90                95


Ser Asn Asn Gly Val Glu Glu Ile Arg Asp Ile Arg Glu Lys Ala Asn
            100                105                110


Tyr Ala Pro Thr Ser Ala Val Tyr Lys Val Tyr Ile Ile Asp Glu Val
        115                120                125


His Met Leu Ser Ser Gly Ala Phe Asn Ala Leu Leu Lys Thr Leu Glu
    130                135                140


Glu Pro Pro Ala Asn Val Val Phe Ile Leu Ala Thr Thr Glu Pro His
145                150                155                160


Lys Ile Pro Ala Thr Ile Ile Ser Arg Thr Gln Arg Phe Asp Phe Lys
                165                170                175
```

Arg Ile Asp Asn Gln Asp Ile Ile Asp Arg Leu Ile Tyr Ile Leu Glu
      180   185   190

Glu Asp Gln Val Pro Tyr Ser Lys Glu Ala Val Leu Ser Leu Ala Asn
      195   200   205

Ala Ala Glu Gly Gly Met Arg Asp Ala Leu Ser Met Leu Asp Gln Ala
      210   215   220

Leu Ser Phe Met Thr Asp Glu Leu Thr Glu Glu Val Ala Leu Gln Ile
225   230   235   240

Thr Gly Ser Ile Thr Gln Ser Leu Leu Leu Glu Tyr Leu Gln Val Ile
            245   250   255

Ser Gln Gly Gln Thr Glu Glu Gly Leu Lys Leu Leu Gln Glu Val Leu
      260   265   270

Gly Glu Gly Lys Asp Pro Ser Arg Phe Val Glu Asp Ala Ile Met Met
      275   280   285

Thr Arg Asp Leu Leu Leu Tyr Gln Thr Ser Gln Gly Asp Asn Phe Val
      290   295   300

Pro Lys Leu Ala Arg Leu Asp Asp Gln Phe Glu Asp Leu Ala Lys Asp
305   310   315   320

Leu Asp Lys Glu Met Ala Tyr His Ile Ile Asp Val Leu Asn Gln Thr
            325   330   335

Gln Asp Asp Leu Arg Leu Ser Asn His Gly Glu Val Tyr Leu Glu Ile
            340   345   350

Ala Thr Val Lys Leu Ser Gln Pro Ser Ser Ala Val Gln Thr Ile Gln
      355   360   365

Ala Ser Gln Val Asn Met Val Asp Gln Asp Asn Lys Glu Glu Ile Ala
      370   375   380

Gln Leu Gln Asn Gln Val Lys Ser Leu Gln Gln Ser Ile Gln Asn Leu
385   390   395   400

```
Gln Ala Gly Ala Lys Gln Gly Pro Lys Gln Arg Ala Lys Ser Lys Ala
            405             410             415

Gly Pro Lys Gln Ser Gly Pro Gly Lys Ser Arg Ser His Arg His Gln
            420             425             430

Gln Gly Phe Lys Val Asn Arg Lys Ala Val Tyr Ser Ile Leu Asp Gln
        435             440             445

Ala Thr Arg Lys Asp Leu Asp Asp Leu Gln Asp Leu Trp Pro Asp Leu
    450             455             460

Ile Asn Val Leu Thr Ile Ser Gln Lys Ala Ile Leu Asn Asn Ser Lys
465             470             475             480

Pro Val Ala Ala Ser Pro Glu Gly Leu Val Val Thr Phe Glu Tyr Asp
            485             490             495

Ile Leu Cys Glu Arg Ala Glu Ser Asp Glu Thr Leu Gln Thr Ala Ile
            500             505             510

Gly Asn Tyr Ile Glu Lys Ile Ile Gly Arg Arg Pro Arg Leu Val Cys
        515             520             525

Val Pro Glu Asp Lys Trp Pro Thr Ile Arg Arg Asp Phe Ile Lys Gln
    530             535             540

Met Lys Lys Glu Asp Gly Ser Thr Lys Ala Gly Gln Ala Ser Asp Gly
545             550             555             560

Lys Ser Asp Asp Asp Pro Gly Gln Glu Asp Asn Gln Ala Leu Asn Lys
            565             570             575

Ala Val Glu Leu Phe Gly Lys Asp Asn Ile Thr Ile Lys Asp
            580             585             590
```